

=> d his

(FILE 'HOME' ENTERED AT 09:59:54 ON 28 NOV 2007)

FILE 'REGISTRY' ENTERED AT 10:00:02 ON 28 NOV 2007

L1 STRUCTURE UPLOADED

L2 0 S L1

FILE 'STNGUIDE' ENTERED AT 10:00:46 ON 28 NOV 2007

FILE 'REGISTRY' ENTERED AT 11:21:30 ON 28 NOV 2007

L3 STRUCTURE UPLOADED

L4 97 S L3 SSS FULL

FILE 'CAPLUS' ENTERED AT 11:22:03 ON 28 NOV 2007

L5 1188 S L4

FILE 'STNGUIDE' ENTERED AT 11:22:10 ON 28 NOV 2007

FILE 'CAPLUS' ENTERED AT 11:23:25 ON 28 NOV 2007

L6 142 S L5 AND PREP/RL

L7 71 S L5 AND (CRYST? OR POLYMORPH? OR XRD? OR X-RAY? OR XRAY OR AMO

L8 186 S L6 OR L7

FILE 'STNGUIDE' ENTERED AT 11:25:41 ON 28 NOV 2007

FILE 'REGISTRY' ENTERED AT 11:27:03 ON 28 NOV 2007

=> d l1

L1 HAS NO ANSWERS

L1 STR

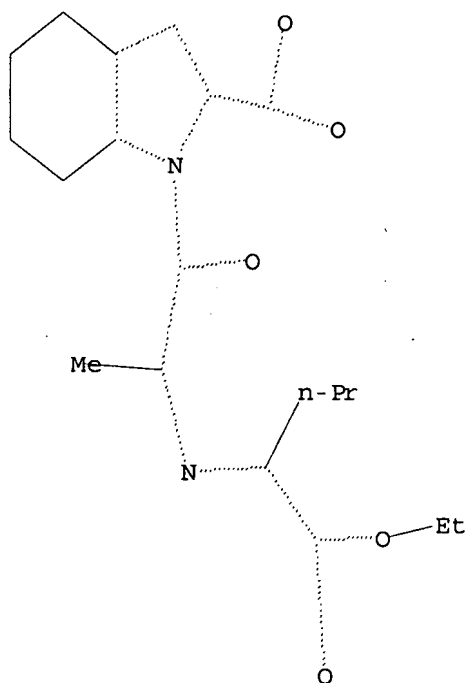
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> d l3

L3 HAS NO ANSWERS

L3 STR



Structure attributes must be viewed using STN Express query preparation.

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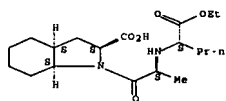
ANSWER 1 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 2007:1245909 CAPLUS Full-text
 TI Test kit for forecasting curative effects of angiotensin-converting enzyme inhibitor
 IN Xing, Houxun; Zhang, Yan; Wang, Binyan; Li, Zhiping; Wu, Di; Zang, Tonghua; Xu, Xiping
 PA Anhui Institute of Biomedical Sciences, Peop. Rep. China
 SO Faming Zhuanli Shengqing Gongkai Shuomingshu, 23pp.
 CODEN: CNXKEV
 DT Patent
 LA Chinese
 FAN: CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 101063166	A	20061031	CN 2006-10011839	20060430
PRAI CN 2006-10011839		20060430		

AB The invention discloses the relationship between single nucleotide polymorphism of prolylcarboxypeptidase (PRCP) E112D site and antihypertensive effects of angiotensin-converting enzyme inhibitor (ACEI). If the genotype is homozygous wild type 112EE, the curative effect of ACEI is good, or else, the curative effects are not obvious. The title test kit comprises polymorphism-typing oligonucleotide for detecting PRCP E112D polymorphism, and related reaction system. The title method is convenient for individual treatment according to individual differences, and can increase curative effects and safety in clinic. The invention can be used for developing anti-hypertension medicines targeting PRCP.

IT INDEXING IN PROGRESS
 IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (test kit for forecasting curative effects of angiotensin-converting enzyme inhibitor)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



ANSWER 2 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 2007:1245908 CAPLUS Full-text
 TI Method for forecasting curative effects of angiotensin-converting enzyme inhibitor
 IN Xing, Houxun; Zhang, Yan; Wang, Binyan; Li, Zhiping; Wu, Di; Zang, Tonghua; Xu, Xiping
 PA Anhui Institute of Biomedical Sciences, Peop. Rep. China

10576386 3 of 361

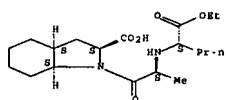
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 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 PRAI US 2006-787936P P 20060331
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 1-Heterocyclylamino-2-hydroxy-3-amino-m-arylalkanes of formula I (wherein R1, R3 is H, halogen, cyano, etc.; R2 is H, (C1-C12)alkyl, etc.; R2 and R3 together can also be part of a ring; R4 is H, lower alkyl, hydroxy, etc.; X is methylene or hydroxymethylene; R5 is lower alkyl, lower haloalkyl, etc.; R6 is amino, lower alkylamino, etc.; R7 is H, lower alkyl, etc.; Q is a an oxothiadiazole or a cyclobutenedione; R8 is lower alkyl, lower haloalkyl, etc.) the salts thereof have renin-inhibiting properties and can be used as antihypertensive, medicinally active ingredients. Methods for preparing the compds. are disclosed. Example compound II was prepared by reacting 3,4-dimethoxycyclobut-3-ene-1,2-dione with a methoxybenzyl heptan-3-carbamate to give III, which was subsequently reacted with benzylamine and deprotected. The compds. of the invention exhibited inhibiting activities in in vitro renin inhibition assays at min. concns. of from approx. 5 x 10⁻⁵ M to approx. 10⁻¹² M.

IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (codrug; preparation of 1-heterocyclylamino-2-hydroxy-3-amino-m-arylalkanes as renin inhibitors for treating hypertension and other diseases)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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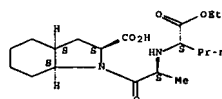
SO Faming Zhuanli Shengqing Gongkai Shuomingshu, 19pp.
 CODEN: CNXKEV
 DT Patent
 LA Chinese
 FAN: CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 101063166	A	20061031	CN 2006-10011836	20060430
PRAI CN 2006-10011836		20060430		

AB The invention discloses the relationship between prolylcarboxypeptidase (PRCP) Glu112Asp (polymorphic site E112D) polymorphism and antihypertensive effects of angiotensin-converting enzyme inhibitor (ACEI, such as benazepril). If the genotype is homozygous wild type 112EE, the curative effect of ACEI is good, or else, the decrease of blood pressure is small. Thus, the polymorphism of PRCP E112D site or the polymorphism of the other PRCP-linked genes can be used for forecasting curative effects of ACEI. The title method is convenient for individual treatment according to individual differences, and can increase curative effects and safety in clinic. The invention can be used for developing anti-hypertension medicines targeting PRCP.

IT INDEXING IN PROGRESS
 IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (method for forecasting curative effects of angiotensin-converting enzyme inhibitor)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



ANSWER 3 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 2007:1237245 CAPLUS Full-text
 TI Preparation of 1-heterocyclylamino-2-hydroxy-3-amino-m-arylalkanes as renin inhibitors for treating hypertension and other renin-mediated diseases
 IN Baldwin, John J.; Claremon, David A.; Dillard, Lawrence W.; Ishchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; McGeehan, Gerard; Zeng, Wenguang
 PA Vitae Pharmaceuticals, Inc., USA
 SO PCT Int. Appl., 89pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN: CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007120523	A2	20071025	WO 2007-US8180	20070330

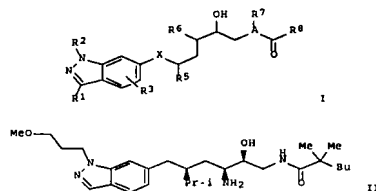
10576386 4 of 361

RE: CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 4 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 2007:1204694 CAPLUS Full-text
 DN 147:486433
 TI 6-(Aminoalkyl)indazoles as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with renin activity
 IN Baldwin, John J.; Claremon, David A.; Dillard, Lawrence W.; Ishchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; McGeehan, Gerard; Zeng, Wenguang
 PA Vitae Pharmaceuticals, Inc., USA
 SO PCT Int. Appl., 75pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN: CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007120523	A2	20071025	WO 2007-US8180	20070330

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 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 PRAI US 2006-788082P P 20060331
 GI



AB 6-(Aminoalkyl)indazoles of formula I and the salts thereof have renin-inhibiting properties and can be used as antihypertensive, and renal, cardiac and vascular protecting medicinally active ingredients. Compds. of formula I

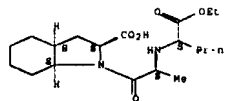
R1 is H, lower (halo)alkyl, (halo)cycloalkyl, amino, CN, etc.; R2 is lower (halo)alkyl, (halo)cycloalkyl, lower (halo)cycloalkylalkyl, lower cyanoalkyl, etc.; R3 is H, CN, and lower (halo)alkyl; X is CH₂, CHOH, and lower alkanoyloxymethylene; R5 is lower (halo)alkyl, (halo)cycloalkyl, lower (halo)alkyl-cycloalkyl, etc.; R6 is amino and lower alkylamino; A is H and CH; R7 is H, lower (halo)alkyl, cycloalkyl, and lower (halo)alkoxy-lower alkyl; R8 is lower (halo)alkyl, C8-15 (halo)alkyl, (halo)cycloalkyl, lower alkylcycloalkyl, etc.; and their enantiomers, diastereoisomers and salts thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their renin inhibitory activity (some data given).

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of aminoalkylindazoles as renin inhibitors useful in treatment of diseases - associated with renin activity)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



✓ NUMBER 6 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2007:1177123 CAPLUS Full-Text

DN 147:469232

TI Acylpiperidine compounds as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with aspartic protease activity

IN Baldwin, John J.; Claremon, David A.; Tice, Colin M.; Cacatian, Salvacion; Dillard, Lawrence W.; Ishchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; McGehean, Gerard; Zhao, Mei; Simpson, Robert D.; Singh, Suresh B.; Flaherty, Patrick J.; Mallander, Lars S.; Leach, Colin A.; Lawhorn, Brian; Lu, Qing; Terrell, Lamont R.; Ghavini-Alagha, Bahman; Zhang, Jing; Ghirlanda, Daniele; Hou, Xiaoping; Semus, Simon

PA Vitas Pharmaceuticals, Inc., USA; Smithkline Beecham Corporation

SO PCT Int. Appl., 41pp.

CODEN: PIXXD2

DT Patent

LA English

FAN, CNT 2

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PI NO 2007117482	A2	20071018	NO 2007-US8339	20070405
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PRAI US 2006-789703P P 20060405

US 2006-789823P P 20060405

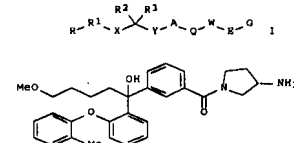
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GQ, GW, GM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, LM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-789703P P 20060405

US 2006-789823P P 20060405

GI



II

AB Disclosed are compds. according to formula I wherein the variables are defined herein. Compds. of formula I wherein R is H, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, C3-7 cycloalkyl, C5-7 cycloalkenyl, etc.; R1 is (un)substituted Ph, (un)substituted (mono/bi)cyclic heteroaryl and (un)substituted C3-7 cycloalkyl; X and Y are independently CH₂ and a single bond; R2 is H, C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C1-12 alkoxy, etc.; R3 is H, halo, C1-6 alkyl, C1-6 alkoxy, OH, etc.; A is (un)substituted (un)saturated (un)bridge 4- to 7-membered ring; Q and Y are attached to carbon or nitrogen in ring A via 1,2- or 1,3- or 1,4-relationship; Q is CO, CS, SO₂, C-CN-NO₂, C=N-CN, dioxocyclobutylene, etc.; W is a bond and (un)substituted C1-5 alkylene; E is (un)substituted (un)saturated (un)bridge 3- to 7-membered ring; G is H, C1-6 alkyl, C4-7 heterocyclyl, OH, NH₂ and deriva., etc.; and their enantiomers, diastereoisomers, and pharmaceutically acceptable salts thereof, are claimed. Such compds. can bind aspartic proteases to inhibit their activity. They are useful in the treatment or amelioration of diseases associated with aspartic protease activity. Also described herein are methods of antagonizing aspartic protease inhibitors in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a compound according to formula I. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their renin inhibitory activity (some data given).

IT 82834-16-0, Perindopril

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(codrug; preparation of acylpiperidine compds. as aspartic protease

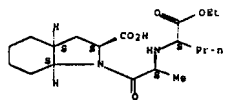
inhibitors including renin inhibitors useful in treatment of diseases -

associated with aspartic protease activity)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



✓ NUMBER 6 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2007:1177123 CAPLUS Full-Text

DN 147:469232

TI Piperidinyl pyrrolidinyl methanone compounds as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with aspartic protease activity

IN Baldwin, John J.; Claremon, David A.; Tice, Colin M.; Cacatian, Salvacion; Dillard, Lawrence W.; Ishchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; McGehean, Gerard; Zhao, Mei; Simpson, Robert D.; Singh, Suresh B.

PA Vitas Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 32pp.

CODEN: PIXXD2

DT Patent

LA English

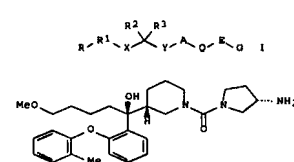
FAN, CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI NO 2007117559	A2	20071018	NO 2007-US8520	20070405
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RM:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GQ, GW, GM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, LM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRAI US 2006-789703P P 20060405

US 2006-789823P P 20060405

GI



II

AB Described are compds. of formula I, which are orally active and bind to aspartic proteases to inhibit their activity. They are useful in the treatment or amelioration of diseases associated with aspartic protease activity. Also described are methods of use of the compds. described herein in ameliorating or treating aspartic protease related disorders in a subject in need thereof. Compds. of formula I wherein R is C1-6 alkyl, C2-8 alkenyl, C2-8 alkynyl, C3-7 cycloalkyl, C2-7 cycloalkenyl, etc.; R1 is Ph, (mono/bi)cyclic heteroaryl, benzo-1,3-dioxole, benzo-1,3-dioxin, etc.; X and Y are independently CH₂ and a single bond; R2 is H, C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C1-12 alkoxy, C1-12 alkylthio, etc.; R3 is H, halo, C1-6 alkyl, C1-6 alkoxy, OH, etc.; A is (un)substituted (un)saturated (un)bridge 4- to 7-membered ring; Q and U are attached to carbon or nitrogen atoms in ring A in a 1,2 or 1,3 or 1,4 relationship; Q is CO, CS, SO₂, C-CN-NO₂, C=N-CN, dioxocyclobutylene, etc.; E is (un)substituted (un)saturated (un)bridge 3- to 7-membered ring; G is OH, C1-6 hydroxyalkyl, amino, C1-6 aminoalkyl, C1-6 (NH)NH₂ and deriva., etc.; and their enantiomers, diastereoisomers and salts thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their renin inhibitory activity.

IT 82834-16-0, Perindopril

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(codrug; preparation of pyrrolidinyl piperidinyl methanone compds. as

aspartic protease inhibitors including renin inhibitors useful in

treatment of diseases - associated with aspartic protease activity)

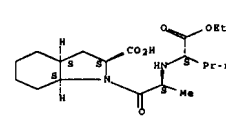
RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-

(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA

INDEX NAME)

Absolute stereochemistry. Rotation (-).



10576386

9 of 361

LS ANSWER 7 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2007:1175935 CAPLUS Full-text

DN 147:480410

TI Thienopyrimidines having Mnk1/Mnk2 inhibiting activity for pharmaceutical compositions
IN Aicher, Babette; Collier, Thomas Stephen; Jaekel, Stefan; Kelter, Arndt-Rene; Murfin, Stephen; Reuter, Tanja; Taylor, Steven
PA Develogen Aktiengesellschaft, Germany
SO PCT Int. Appl., 95pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007/115822	A1	20071018	WO 2007-EP3186	20070410
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI EP 2006-7454

A 20060407

AB The present invention relates to novel pharmaceutical compns. comprising thienopyrimidine compds. Moreover, the present invention relates to the use of the thienopyrimidine compds. of the invention for the production of pharmaceutical compns. for the prophylaxis and/or treatment of diseases which can be influenced by the inhibition of the kinase activity of Mnk1 and/or Mnk2 (Mnk2a or Mnk2b) and/or variants thereof. The present invention is more particularly directed to the treatment and/or prophylaxis of in particular metabolic diseases of the lipid and carbohydrate metabolism and the consecutive complications and disorders associated therewith.

IT 82834-16-0, Perindopril

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

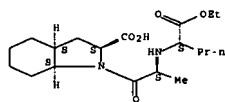
(Biological study); USES (Uses)

(thienopyrimidines having Mnk1/Mnk2 kinase inhibiting activity for pharmaceutical compns. for treating disease and combination with other agents)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



10576386

11 of 361

AB Described are compds. of formula I which are orally active and bind to renin to inhibit its activity. Compds. of formula I wherein G1 is Cl-9 (halo)alkyl, C3-7 (halo)cycloalkyl, C4-9 (halo)cycloalkylalkyl, Ph, etc.; G2 is H, C1-8 (fluoro)alkyl, C4-8 (fluoro)cycloalkylalkyl, C1-8 (fluoro)alkoxy, etc.; G3 is H, halo, OH, C1-4 alkanoylamino, and C1-3 alkoxy; A4 is CH2 and O; Q is CO, CS, SO2, C=C, NO2, C=N, CO, etc.; T is a mimic of the Leu-Val cleavage site of angiotensinogen, and their enantiomers, diastereoisomers, and salts thereof, are claimed. They are useful in the treatment or amelioration of diseases associated with renin activity. Also described are methods of use of these compds. for treating or ameliorating a renin mediated disorder in a subject. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their renin inhibitory activity.

IT 82834-16-0, Perindopril

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

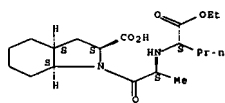
(Biological study); USES (Uses)

(codrug; preparation of piperidine and morpholine compds. as renin inhibitors useful in treatment of diseases - associated with aspartic protease and renin activity)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LS ANSWER 9 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2007:971549 CAPLUS Full-text

DN 147:330200

TI Beta crystalline form of the salt of perindopril arginine, its preparation process, and pharmaceutical compositions containing it
IN Coquerel, Gerard; Lefebvre, Loic; Souvie, Jean Claude; Authouart, Pascale
PA Les Laboratoires Servier, Fr.
SO Fr. Demande, 12pp.
CODEN: FRXXBL

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 2897865	A1	20070831	FR 2006-1747	20060228
WO 2007099216	A2	20070907	WO 2007-FR334	20070226
WO 2007099216	A3	20071025		
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

10576386

10 of 361

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 8 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2007:1175900 CAPLUS Full-text

DN 147:469351

TI Piperidines and morpholines as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with renin activity

IN Baldwin, John J.; Claremont, David A.; Tice, Colin M.; Cacciatore, Salvatore; Dillard, Lawrence W.; Ishchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; McGehean, Gerard; Zhao, Wei; Simpson, Robert D.; Singh, Suresh B.

PA Vitae Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 222pp.

CODEN: PIXXD2

DT Patent

LA English

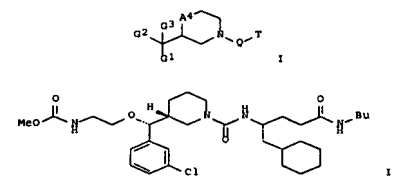
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007/117560	A2	20071018	WO 2007-US8521	20070405
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PRAI US 2006-789723P

P 20060405

GI



10576386

12 of 361

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI FR 2006-1747

A 20060228

AB Beta crystalline form of arginine salt of perindopril characterized by its x-ray diffraction pattern as a powder is claimed. Arginine salt of perindopril was crystallized from acetonitrile and dried to obtain the beta crystalline form. Formulation of a tablet containing 4 mg of the above salt is disclosed.

IT 612548-45-5

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(beta crystalline form of salt of perindopril arginine, its preparation process, and pharmaceutical compns. containing it)

RN 612548-45-5 CAPLUS

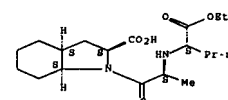
CN L-Arginine, (2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

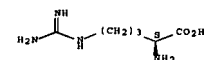


CM 2

CRN 74-79-3

CMF C6 H14 N4 O2

Absolute stereochemistry.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 10 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2007:971548 CAPLUS Full-text
 DN 147:330199
 TI Alpha crystalline form of the salt of perindopril arginine, its preparation process, and pharmaceutical compositions containing it
 IN Coquerel, Gerny, Lefebvre, Loic; Souvire, Jean Claude; Authouart, Pascale
 PA Les Laboratoires Servier, Fr.
 SO Fr. Demande, 13pp.
 CODEN: PRXBL
 DT Patent
 LA French
 FAN.CNT 1

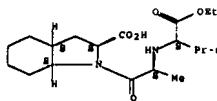
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 200709217	A1	20070907	WO 2007-FR335	20070226
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RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GN, GO, GM, ML, MR, NE, SN, TD, TO, BM, GH, KE, LB, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRAI FR 2006-1748 A 20060228
 AB Alpha crystalline form of arginine salt of perindopril characterized by its x-rays diffraction pattern as a powder is claimed. Arginine salt of perindopril prepared by the reaction of L-arginine with perindopril. Formulation of a tablet containing 4 mg of the above salt is disclosed.

IT 612549-46 ?
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (alpha crystalline form of salt of perindopril arginine, its preparation process, and pharmaceutical compns. containing it)
 RN 612549-45-5 CAPLUS
 CN L-Arginine, (2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:1) (CA INDEX NAME)

CM 1
 CRN 82834-16-0
 CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

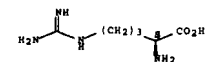


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 WO 2005112870 A1 20051201 WO 2005-US18638 20050523
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 CA 2566310 A1 20060113 CA 2005-2566310 20050523
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 WO 2006038916 A2 20060413 WO 2005-US18632 20050523
 WO 2006038916 A3 20060101
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EP 1746979 A2 20070131 EP 2005-825029 20050523
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 EP 1750647 A1 20070214 EP 2005-754113 20050523
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 EP 1755560 A1 20070228 EP 2005-754171 20050523
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 EP 1755564 A2 20070228 EP 2005-754425 20050523

CM 2
 CRN 74-79-3
 CMP C6 H14 N4 O2

Absolute stereochemistry.



RE.CNT THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 11 OF 186 CAPLUS COPYRIGHT 2007 ACS on 87N
 AN 2007:912792 CAPLUS Full-text
 DN 147:243411
 TI Pharmaceutical tablets with active and inactive segments
 IN Solomon, Lawrence; Kaplan, Allan S.
 PA USA
 SO U.S. Pat. Appl. Publ., 30pp., Cont.-in-part of U.S. Ser. No. 569,343.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 7

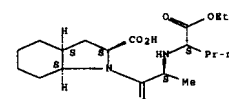
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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AU 2005245026	A1	20051201	AU 2005-245026	20050523
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AU 2005245028	A1	20051201	AU 2005-245028	20050523
CA 2564960	A1	20051201	CA 2005-2564960	20050523
CA 2564961	A1	20051201	CA 2005-2564961	20050523
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WO 2005112900	A1	20051201	WO 2005-US18631	20050523
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WO 2005112897	A2	20051201	WO 2005-US18633	20050523
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 CN 1960712 A 20070509 CN 2005-80016365 20050523
 CN 1964703 A 20070516 CN 2005-80016366 20050523
 CN 1993111 A 20070704 CN 2005-80016277 20050523
 CN 1997331 A 20070711 CN 2005-80016276 20050523
 US 2007031488 A1 20070208 US 2006-441456 20060525
 IN 2006KN03322 A 20070615 IN 2006-KN3322 20061113
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 IN 2006KN03324 A 20070615 IN 2006-KN3324 20061113
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 US 2004-573134P P 20040521
 WO 2005-US18631 W 20050523
 WO 2005-US18632 W 20050523
 WO 2005-US18633 W 20050523
 WO 2005-US18638 W 20050523
 WO 2005-US18639 W 20050523
 US 2006-598267 A2 20060823
 US 2006-598306 A2 20060824
 US 2006-598315 A2 20060824
 US 2006-598344 A2 20060824
 US 2006-569343 A2 20061117

AB An immediate release compressed pharmaceutical tablet that has 2 or more segments and a top and a bottom and has a height that exceeds the width of the tablet. The height is measured vertically from the top to the bottom of the tablet while it is in the tablet die in which it is fully compressed, after compression has been completed. The width is measured as the greatest horizontal dimension of the tablet at a location halfway between the top and the bottom of the tablet, except that when the horizontal cross-section of the tablet is substantially rectangular, the width is defined by locating the two shorter sides of the perimeter of the horizontal cross-section, and measuring the length of a line that is at right angle to the shorter sides.

IT 82834-16-0, Perindopril
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical tablets with active and inactive segments)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



ANSWER 12 OF 186 CAPLUS COPYRIGHT 2007 ACS on 87N
 AN 2007:912292 CAPLUS Full-text
 DN 147:243172

TI Crystalline forms of perindopril erbumine
 IN Devarakonda, Surya Narayana; Asnani, Minakshi; Bonnareddy, Sivakumarr
 Reddy, Pad; Pratap Reddy; Chandramohan, Udhaya Kumar; Chitre, Saurabh
 Shashikanth; Nalivella, Venu; Vasamsetti, Satish Kumar
 PA Dr. Reddy's, USA
 SO PCT Int. Appl., 27pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007092758	A2	20070816	WO 2007-US61524	20070202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MM, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI IN 2006-CH177	A	20060203		
US 2006-803087P	P	20060524		
IN 2006-CH970	A	20060606		
US 2006-821178P	P	20060802		
IN 2006-CH1507	A	20060824		
US 2006-868597P	P	20061205		

AB Crystalline forms ζ - and η - of perindopril erbumine are described. Perindopril erbumine was mixed with MeOH for 10 min and the solution was allowed to evaporate slowly to give ζ - form of the compound

IT 107133-36-8, Perindopril erbumine
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (crystalline forms of perindopril erbumine)

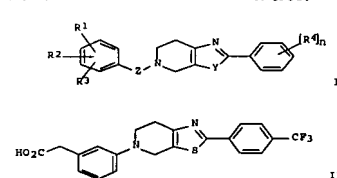
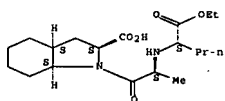
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



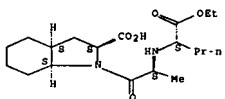
AB The title compds. I [n = 0-2; R1 = XCO2R13, OCR11R12XCO2R13 (wherein X = a bond or alkylene; R11, R12 = H, alkyl or alkoxy; or R11 and R12 together with the carbon atom to which R11 and R12 are attached form cycloalkyl; R13 = H, alkyl); R2, R3 = H, halo, alkyl, etc.; Z = a bond, S(O)0-2; Y = O, S; R4 = H, halo, alkyl, etc.], useful as PPAR modulators for treating and preventing PPAR-mediated diseases (no specific data), were prepared Thus, coupling 2-(4-trifluoromethylphenyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine with Me (3-bromophenyl)acetate (prepn. given) followed by treating the resulting ester with LiOH afforded 44% II (over 2 steps). The invention relates also to pharmaceutical compns. comprising compds. I and methods of using such compds. to treat or prevent diseases or disorders associated with the activity of the Peroxisome Proliferator-Activated Receptor (PPAR) families.

IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of substituted thiazolopyridines as PPAR modulators useful in treatment and prevention of PPAR-mediated diseases)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 14 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

2007:873324 CAPLUS Full-text

DN 147:257757

TI Preparation of substituted thiazolyl tetrahydroisquinolines as PPAR modulators

CM 2

CRN 75-64-9
 CMF C4 H11 N

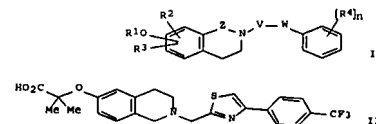


ANSWER 13 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 2007:874469 CAPLUS Full-text
 DN 147:257759
 TI Preparation of substituted thiazolopyridines as PPAR modulators
 IN Epplé, Robert; Russo, Ross; Azimioara, Mihai
 PA IRM LLC, Bermuda
 SO PCT Int. Appl., 40pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007089667	A1	20070809	WO 2007-US2316	20070125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MM, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2006-763539P	P	20060130		
OS MARPAT 147:257759				
GI				

IN Epplé, Robert; Cow, Christopher
 PA IRM LLC, Bermuda
 SO PCT Int. Appl., 47pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007089557	A2	20070809	WO 2007-US2115	20070125
WO 2007089557	A3	20071108		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MM, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, P, EA, EP, OA				
PRAI US 2006-763623P	P	20060130		
OS MARPAT 147:257757				
GI				



AB The title compds. I [n = 0-2; R1 = CR11R12XCO2R13 (wherein X = a bond or alkylene; R11, R12 = H, alkyl, alkoxy; or R11 and R12 together with the carbon atom to which R11 and R12 are attached form cycloalkyl; R13 = H, alkyl); R2, R3 = H, alkyl; V = a bond, alkylene, CONR8, X1C(O)X2 (X1, X2 = a bond, alkylene; R8 = H, alkyl); W = (un)substituted thiazole, oxazole, Z = CH2, C(O); R4 = H, halo, alkyl, etc.], useful as PPAR modulators for treating and preventing PPAR-mediated diseases (no specific data given), were prepared Thus, reacting Me 2-(1,2,3,4-tetrahydroisquinolin-6-yloxy)-2-methylpropanoate with 2-(chloromethyl)-4-(4-trifluoromethylphenyl)thiazole followed by treatment of the resulting ester with LiOH and then acidification, afforded the acid II. The invention relates also to pharmaceutical compns. comprising compds. I and methods of using such compds. to treat or prevent diseases or disorders associated with the activity of the Peroxisome Proliferator-Activated Receptor (PPAR) families.

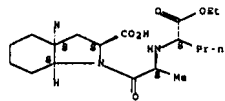
IT 82834-16-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted thiazolyl tetrahydroisoquinolines as PPAR modulators useful in treatment and prevention of PPAR-mediated diseases)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



✓ ANSWER 16 OF 166 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2007:845244 CAPLUS Full-text

DN 147:212285

TI Process for the preparation of N-[1-(S)-ethoxycarbonyl-1-butyl]-L-alanine-(S)-alanine-DMT complex and its use in the preparation of perindopril

IN Joshi, Narendra Shriram; Pradhan, Nitin Sharad Chandra

PA Glenmark Pharmaceuticals Limited, India

SO PCT Int. Appl., 16pp.

CODEN: PIXX02

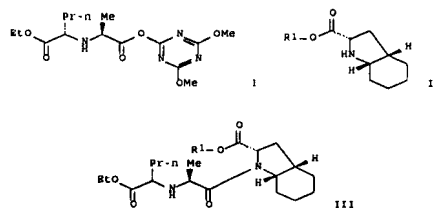
DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI NO 2007085933	A2	20070802	NO 2007-18150	20070123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, ML, PL, PT, RO, SE, SI, SK, TK, TR, BF, BJ, CF, CG, CI, CM, GA, GM, GG, GN, GW, HK, HN, IL, IN, JP, KE, KG, KH, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				

PRAI IN 2006-MU125 A 20060225
US 2006-792875P P 20060218
OS CARREACT 147:212285; MARPAT 147:212285
GI



AB A process for the preparation of N-[1-(S)-ethoxycarbonyl-1-butyl]-L-alanine-DMT complex (I) by reaction of N-[1-(S)-ethoxycarbonyl-1-butyl]-L-alanine with 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride in a solvent and its use in the synthesis of perindopril, perindopril erbiumine or pharmaceutically acceptable salts by reaction of I with compound (II) (R1 = aryl, alkyl, or silyl protective group) in a solvent, following by deprotection of compound (III) using suitable deprotecting agent, is described. Thus, N-[1-(S)-ethoxycarbonyl-1-butyl]-L-alanine and 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride were mixed in THF and stirred for about 10 min at t° = 20-25° under nitrogen. To the resulting solution contained complex I was added (2S, 3aS, 7aS)-benzyl-perhydroindole-2-carboxylate at t° = 20-25° under nitrogen, and after separation and purification 1.5 g of perindopril benzyl ester was obtained, which was transformed into perindopril tert-Bu amine salt.

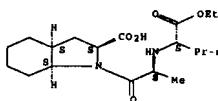
IT 82834-16-0P, Perindopril 107133-36-SP
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of ethoxycarbonylbutyl alanine DMT complex and its use in preparation of perindopril and perindopril erbiumine)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-

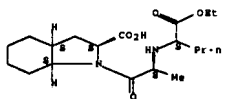
(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (111) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N



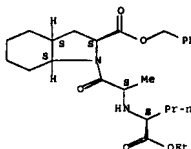
IT 122454-52-4P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of ethoxycarbonylbutyl alanine DMT complex and its use in preparation of perindopril and perindopril erbiumine)

RN 122454-52-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



✓ ANSWER 16 OF 166 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2007:845231 CAPLUS Full-text

DN 147:235167

TI Spiro imidazole derivatives as PPAR modulators and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with PPAR activity.

IN Epple, Robert; Russo, Ross; Azimioara, Mihai; Cow, Christopher; Molteni, Valentin; Li, Xiaolin; Chianelli, Donatella

PA IRM LLC, Nevada

SO PCT Int. Appl., 101pp.

CODEN: PIXX02

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI NO 2007087448	A1	20070802	NO 2007-US2315	20070125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, ML, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GM, GG, GN, GW, HK, HN, IL, IN, JP, KE, KG, KH, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				

PRAI US 2006-763557P P 20060130

OS MARPAT 147:235167

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides compds. I and II, pharmaceutical compns. comprising such compds. and methods of using such compds. to treat or prevent diseases or disorders associated with the activity of the Peroxisome Proliferator-Activated Receptor (PPAR) families. Compds. of formula I and II wherein A is (un)substituted Ph and (un)substituted thiazol-2-yl; n and m are independently 1 - 5; each R1 is independently H, halo, C1-6 (halo)alkyl, and C1-6

(halo)alkoxy; R3 is C1-8 alkyl, C2-8 alkenyl, C1-6 haloalkyl, C2-6 haloalkenyl, etc.; R4 and R5 are independently H and C1-6 alkyl; or R4R5 taken together to form -O-; Y is N and CH; Z is a bond, SOO-2, CH2, etc.; A and B are independently CH and N; R6 and R7 are independently H, halo, C1-6 (halo)alkyl and C1-6 (halo)alkoxy; R8 is CO2H and derivs., C1-4 alkylene-CO2H and derivs., etc.; R9 and R10 are independently H, C1-6 alkyl, and OH and derivs.; and their pharmaceutically acceptable salts, hydrates, solvates, isomers and prodrugs thereof, are claimed. Example compound III was prepared by N-alkylation of 3-isobutyl-1-[2-(4-methoxyphenyl)ethyl]-1,3,8-triazaspiro[4.5]decane-2,4-dione with Et 3-bromomethylphenylacetate followed by hydrolysis. All the invention compds. were evaluated for their PPAR modulatory activity (some data given).

IT 107133-36-8, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of spiro imidazole deriva. as PPAR receptor modulators useful in treatment and prevention of diseases - associated with PPAR receptors activity)

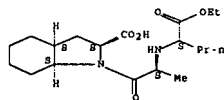
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



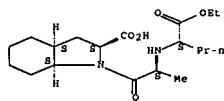
RE.CMT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

monohydrate, 1.3 mg magnesium stearate, 9 mg povidone, 0.3 mg anhydrous colloidal silica, 30 mg cellulose sodium glycolate, and 2.6 mg stearic acid. A great reduction in systolic and diastolic arterial pressure was observed in clin. studies with hypertensive patients.

IT 82834-16-0, Perindopril 107133-36-8 612548-45-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sinus node current inhibitor ivabradine association with an angiotensin converting enzyme inhibitor and pharmaceutical compns. containing it for treating arterial hypertension)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

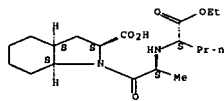
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N

ANSWER 17 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:675141 CAPLUS Full-text

DN 147:79625

TI Association of a sinus node If current inhibitor, ivabradine, with an angiotensin converting enzyme inhibitor, and pharmaceutical compositions containing it for treating arterial hypertension

IN Benatar, J.; Lerebours-Pigeonniere, Guy

PA Les Laboratoires Servier, Fr.

SO U.S. Pat. Appl. Publ., 6pp.

CODEN: USXXCO

DT Patent

LA English

FAN: CWT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007142355	A1	20070621	US 2006-642899	20061220
FR 2894825	A1	20070622	FR 2005-13006	20051221
SG 133545	A1	20070730	SG 2006-8805	20061218
NO 2006005905	A	20070622	NO 2006-5905	20061219
IN 2006DE02713	A	20070803	IN 2006-DE2713	20061219
EP 1800678	A1	20070627	EP 2006-291993	20061220
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
WO 2007077327	A1	20070712	WO 2006-FR2803	20061220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MM, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BP, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2571644	A1	20070621	CA 2006-2571644	20061221
KR 2007066921	A	20070627	KR 2006-131721	20061221
AU 2006252210	A1	20070705	AU 2006-252210	20061221
JP 2007169283	A	20070705	JP 2006-343823	20061221
CN 101015557	A	20070815	CN 2006-10064318	20061221
BR 2006005517	A	20071016	BR 2006-5517	20061221
PRAI FR 2005-13006	A	20051221		

AB The present invention relates to a new association comprising a selective and specific sinus node If current inhibitor, more especially ivabradine, and an agent that inhibits angiotensin-converting enzyme. Angiotensin-converting enzyme inhibitors are one of the major therapeutic classes in the treatment of arterial hypertension. It has been now discovered that selective and specific sinus node If current inhibitors, more especially ivabradine, are capable of potentiating the effects of agents that inhibit angiotensin-converting enzyme. The invention relates more especially to the association between ivabradine, or one of its hydrates, crystalline forms and addition salts with a pharmaceutically acceptable acid, more especially its hydrochloride, and perindopril, or one of its hydrates, crystalline forms and addition salts with a pharmaceutically acceptable base, more especially its arginine or tert-butylamine salt. Medicinal products containing such association which are useful in treating arterial hypertension are described. Thus, pharmaceutical composition of antihypertensive tablets was formulated comprising 7.5 mg ivabradine hydrochloride, 2 mg perindopril tert-butylamine, 62 mg lactose



RN 612548-45-5 CAPLUS

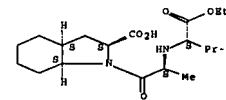
CN L-Arginine, (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:1) (CA INDEX NAME)

CM 1

CRN. 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

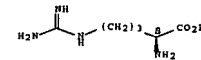


CM 2

CRN 74-79-3

CMF C6 H14 N4 O2

Absolute stereochemistry.



ANSWER 18 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:647580 CAPLUS Full-text

DN 147:88914

TI Use of methylenetetrahydrofolate reductase gene polymorphisms in predicting homocysteine level, homocysteine-associated disease risks, and angiotensin converting enzyme inhibitor-related drug treatment responses in humans

IN Xu, Xiping; Fang, Zhian; Jiang, Shanguo; Wang, Binyan; Yang, Jianhua; Zhang, Zhanchun; Mao, Guangyun; Xing, Houkun; Liu, Ping; Wang, Yan; Zang, Tonghua; Wang, Mengde; Wang, Yu; Dai, Chengxiang; Zhang, Kerong

PA US

SO U.S. Pat. Appl. Publ., 32pp.

CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007134709	A1	20070614	US 2006-638634	20060213
CM 1982471	A	20070620	CN 2005-1010528	20051214
CN 101037708	A	20070919	CN 2006-10064915	20060317
PRAI CN 2005-1010528	A	20051214		
CN 2006-10064915	A	20060317		
CN 2006-10090093	A	20060627		

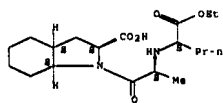
AB This invention features our discovery on usages of methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms in predicting homocysteine (Hcy) level and/or incidence and prognosis of diseases associated with increased Hcy level in a subject, as well as predicting treatment effects of medicines in the category of Angiotensin converting enzyme inhibitor (ACEI) with and without combination with B Vitamins. Polymorphisms within gene MTHFR that are analysed in this invention include nucleotides C677T, A1298C, G1793A, G215A, G482A, and A1317G. This invention also features our discovery on laboratory and anal. methods that are essential to the above described usages of MTHFR gene polymorphisms. In addition, this invention features a kit that has translated the above discoveries into a practical and reliable tool that can be applied to accomplish the above described usages of MTHFR gene polymorphisms. This invention represents an important step in realizing personalized medicine, with the goal to tailor diagnosis, prevention and treatment strategy to meet individual needs.

IT 82834-16-0, Perindopril
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (use of human gene MTHFR polymorphisms in predicting homocysteine level, homocysteine-associated disease risks, and ACEI-related treatment responses)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LE ANSWER 19 OF 106 CAPLUS COPYRIGHT 2007 ACS ON STM

AN 2007:619669 CAPLUS Full-text

DN 147:30943

TI Process for the preparation of perindopril using purified N-[(S)-1-carbethoxybutyl]- (S)-alanine and/or (2S,3aS,7aS)-octahydroindole-2-carboxylic acid or activated or protected forms thereof.
 IN Chen, Weiren; Shi, Jiaxiang; Lu, Biao

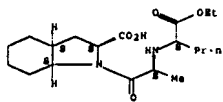
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LE ANSWER 30 OF 106 CAPLUS COPYRIGHT 2007 ACS ON STM

AN 2007:663460 CAPLUS Full-text

DN 146:528317

TI Preparation of stable formulation of amorphous perindopril salts and their use in the therapy of hypertension
 IN Rucman, Rudolf; Zupet, Pavel
 PA Diagen Smartopri Ljubljani, D.O.O., Slovenia

SO PCT Int. Appl., 34pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007058634	A1	20070524	WO 2006-8134	2006108

W: AR, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,

PA Krka, Tovarna Zdravil, D.D., Novo Mesto, Slovenia
 SO PCT Int. Appl., 27pp.
 CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007062865	A1	20070607	WO 2006-EP11558	20061201

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP 1792896 A1 20070606 EP 2005-26160 20051201

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

PRAI EP 2005-26160 A 20051201

SI 2004-143 A 20040514

AB A process for the preparation of (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid uses purified intermediates N-[(S)-1-carbethoxybutyl]- (S)-alanine and/or (2S,3aS,7aS)-octahydroindole-2-carboxylic acid or activated or protected forms thereof, wherein the purified form has been prepared using THF, di-Me carbonate, di-Et carbonate, 1,2-dimethoxyethane, tert-Bu Me ether, 2-methyltetrahydrofuran, cyclopentyl Me ether, or mixts. thereof.

IT 82834-16-0P, Perindopril 107133-36-EP, Perindopril

erbumine

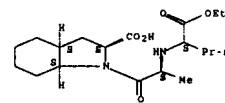
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of perindopril using purified carbethoxybutylalanine and/or octahydroindolecarboxylic acid or activated or protected forms thereof)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

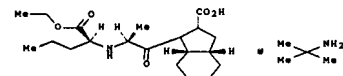
MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI SI 2005-314 A 20051117

SI 2006-177 A 20060731

GI



AB There is disclosed a stable formulation of amorphous perindopril erbumine (I) which is obtained in such a way that I, which may also be prepared in situ from perindopril and tert-butylamine, or I hydrate is dissolved in demineralized water or in a mixture of demineralized water and alc., to this solution a solution of sodium hydrogen carbonate is added for stabilization, inert ingredients for tableting are wetted therewith, dried in vacuo by lyophilization or at normal pressure with a stream of warm air at not more than 40°, hydrophobic additives to facilitate tableting are added, it is homogenized and the granulate is tabletted. Disclosed is also a stable formulation of amorphous perindopril sodium salt obtained by modification of the drying procedure in the process of preparing the granulate. X-ray powder diffraction investigations show that I is present in amorphous form and does not contain crystals α, β and γ forms.

IT 107133-36-SP, Perindopril erbumine 690267-97-1P
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (preparation of stable formulation of amorphous perindopril salts and their use in therapy of hypertension)

RN 107133-36-8 CAPLUS

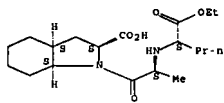
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMP C4 H11 N

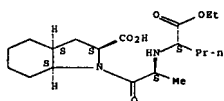
RN 690267-97-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMP C4 H11 N

ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 21 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

RN 2007:538695 CAPLUS Full-text

DN 146:521789

TI Oxazoles and thiazoles as PPAR modulators, their preparation,

pharmaceutical compositions, and use in therapy

IN Epple, Robert; Cow, Christopher; Azimioara, Mihai; Russo, Ross; Xie,

Yongping; Tang, Xing

PA IRM LLC, Bermuda

SO PCT Int. Appl., 139pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007056366	A2	20070518	WO 2006-US43342	20061107
WO 2007056366	A3	20070705		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZM, ZW			
RM:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
PRAI US 2005-734683P	P	20051107		
OS MARPAT 146:521789				
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to oxazoles and thiazoles of formula I, which modulate the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPAR δ . In compds. I, W is O or S; R1 is -L1-X-C(R7R8)-L2-CO2R9; L1 and L2 are independently a bond or C1-4 alkylene; X is a bond, O, or S; R7 and R8 are independently H, C1-4 alkyl, or C1-4 alkoxy; R9 is H or C1-6 alkyl; p is 0-3; each R2 is independently selected from halo, C1-6 alkyl, C2-6 alkenyl, C1-4 alkoxy, C1-4 alkylthio, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; n is 0-3; R3 and R4 are independently H or C1-6 alkyl; R5 and R6 are independently selected from H, C1-6 alkyl, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13 heteroaryl; Y is O, S, NR10, or CR10R11; Z is C10R11 or S; and R10 and R11 are independently selected from H and C1-6 alkyl, including salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I with one or more pharmaceutically acceptable excipients, optionally containing another active ingredient selected from antidiabetic agents, hypolipidemic agents, antioesity agents, antihypertensive agents, etc., as well as to the use of the compns. for the



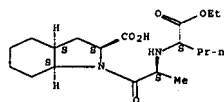
IT 82834-16-0, Perindopril

RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of stable formulation of amorphous perindopril salts and their use in therapy of hypertension)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



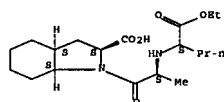
IT 869954-02-6P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PRSP (Preparation); USES (Uses)
(preparation of stable formulation of amorphous perindopril salts and their use in therapy of hypertension)

RN 869954-09-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, sodium salt (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



No

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

treatment or prevention of disease or disorders associated with PPAR activity. Regioselective acetylation of Et (2-methylphenoxy)acetate followed by Baeyer-Villiger oxidation, methanolysis, and regioselective bromination gave phenoxyacetate II, which underwent O-silylation, Suzuki coupling with cyclopropylboronic acid, and desilylation resulting in the formation of cyclopropylphenoxyacetate III. Substitution of 3-chloropropanol with potassium cyanide followed by sulfolysis to the thioamide and heterocyclization with 2-bromo-1-(4-trifluoroethylphenyl)ethanone formed thiazole IV, which was coupled to III under Mitsunobu conditions and hydrolyzed to give thiazole V. The compds. of the invention, e.g., V, are modulators of PPAR, particularly PPAR δ (no data).

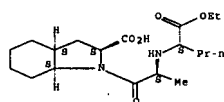
IT 82834-16-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of oxazole and thiazole compds. as PPAR modulators)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



ANSWER 22 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

RN 2007:538194 CAPLUS Full-text

DN 146:521786

TI Oxazoles and thiazoles as PPAR modulators, their preparation,

pharmaceutical compositions, and use in therapy

IN Epple, Robert; Cow, Christopher; Azimioara, Mihai; Russo, Ross

PA IRM LLC, Bermuda

SO PCT Int. Appl., 62pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007056496	A1	20070518	WO 2006-US43586	20061107
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZM, ZW			
RM:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			

OM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM
 PRAI US 2005-734678P P 20051107
 OS MARPAT 146:521786
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to oxazoles and thiazoles of formula I, which modulate the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPAR δ . In compds. I, W is O or S; R₁ is -L1-X-C(R₈R₉)-L2-CO₂R₁₀; L1 and L2 are independently a bond or C1-4 alkylene; X is a bond, O, or S; R₈ and R₉ are independently H, C1-4 alkyl, or C1-4 alkoxy; R₁₀ is H or C1-6 alkyl; p is 0-3; each R₂ is independently selected from halo, C1-6 alkyl, C2-6 alkenyl, C1-4 alkoxy, C1-4 alkylthio, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; n is 0-3; R₃ and R₄ are independently H or C1-6 alkyl; R₅ and R₆ are independently selected from H, C1-6 alkyl, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13 heteroaryl; R₇ is H, C1-6 alkyl, -L3-C6-12 aryl, -L3-C3-12 cycloalkyl, -L3-OR₁₁, or -L3-N(R₁₁R₁₂); L₃ is a bond or C1-4 alkylene; and R₁₁ and R₁₂ are independently H or C1-6 alkyl, including salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I with one or more pharmaceutically acceptable excipients, optionally containing another active ingredient selected from anti-diabetic agents, hypolipidemic agents, anti-obesity agents, anti-hypertensive agents, etc., as well as to the use of the compns. for the treatment or prevention of disease or disorders associated with PPAR activity. Regioselective bromination of 4-benzoyloxyphenol followed by O-allylation, substitution with tetramethyltin, and desilylation gave 4-benzoyloxy-2-methylphenol, which underwent substitution of Me 2-bromo-2-methylpropionate, debenzoylation, and substitution of 1,2-dibromomethane resulting in the formation of ester II. Heterocyclization of 2-bromo-1-(4-(trifluoromethyl)phenyl)ethanone with thiourea formed aminothiazole III, which underwent substitution of bromide II, N-methylation, and ester hydrolysis to give thiazole IV. The compds. of the invention, e.g., IV, are modulators of PPAR, particularly PPAR δ (no data).

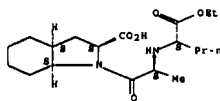
IT 22834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); US&S (Uses)
 (codrug; preparation of oxazole and thiazole compds. as PPAR modulators)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

alkyl; n is 0-3; each R₂ is independently selected from halo, C1-4 alkyl, C1-4 alkoxy, C1-4 alkylthio, and C3-12 cycloalkyl; R₃ is C1-8 alkyl; and R₄ is selected from halo, C1-4 alkyl, C1-4 haloalkyl, and C1-4 haloalkoxy; including salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I with one or more pharmaceutically acceptable excipients, optionally containing another active ingredient selected from anti-diabetic agents, hypolipidemic agents, anti-obesity agents, anti-hypertensive agents, etc., as well as to the use of the compns. for the treatment or prevention of disease or disorders associated with PPAR activity. Diazotization of 4-(trifluoromethoxy)acetophenone followed by heterocyclization with acetonitrile, and sequential double bromination gave dibromooxazole II. O-benzoylation of 4-hydroxybenzaldehyde, condensation with Et ethoxyacetate, and hydrogenation resulted in the formation of ethoxypropionate III, which underwent substitution of II followed by Suzuki coupling with 2-isopropoxy-5-pyrimidinylboronic acid (two-step preparation from 5-bromo-2-chloropyrimidine is given) and ester hydrolysis to give oxazole IV. The compds. of the invention, e.g., IV, are modulators of PPAR, particularly PPAR δ (no data).

IT 22834-16-0
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); US&S (Uses)
 (codrug; preparation of oxazole and thiazole compds. as PPAR modulators)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

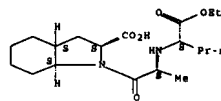
Absolute stereochemistry. Rotation (-).



RE CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 24 OF 166 CAPLUS COPYRIGHT 2007 ACS on STM
 AN 2007:485597 CAPLUS Full-text
 DN 146:482092
 TI Combination of a dipeptidyl peptidase-4 inhibitor and an anti-hypertensive agent for the treatment of diabetes and hypertension
 IN Hasegawa, Philip A.
 PA Merck & Co., Inc., USA
 SO PCT Int. Appl., 42pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI MO 2007050485	A2	20070503	MO 2006-US41233	20061020



RE CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 23 OF 166 CAPLUS COPYRIGHT 2007 ACS on STM
 AN 2007:536876 CAPLUS Full-text
 DN 146:521785
 TI Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
 IN Apple, Robert; Xie, Yongping; Wang, Xing; Russo, Ross; Cow, Christopher; Azimioara, Mihai
 PA IRM LLC, Bermuda
 SO PCT Int. Appl., 80pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN CNT 1

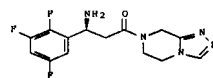
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI MO 2007056497	A1	20070518	WO 2006-US43587	20061107

M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MD, ME, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, CH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 PRAI US 2005-734592P P 20051107
 OS MARPAT 146:521785
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to oxazoles and thiazoles of formula I, which modulate the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPAR δ . In compds. I, W is H or CH; Y is O, S, CH₂CH₂, or CR₅R₆, where R₅ and R₆ are independently selected from H and C1-6 alkyl; Z is S or O; R₁ is -L1-X-C(R₇R₈)-L2-CO₂R₉; L1 and L2 are independently a bond or C1-4 alkylene; X is a bond, O, or S; R₇ and R₈ are independently H, C1-4 alkyl, or C1-4 alkoxy; or R₇ and R₈, together with the carbon atom to which they are attached, form C3-12 cycloalkyl; R₉ is H or C1-6

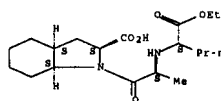
MO 2007050485 A3 20070927
 M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MD, ME, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, CH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, JP, EA, KP, OA
 PRAI US 2005-730167P P 20051025
 GI



AB The invention relates to pharmaceutical compns. comprising a combination of a particular dipeptidyl peptidase-4 (DPP-4) inhibitor I and an anti-hypertensive agent selected from the group consisting of an angiotensin II receptor antagonist and an angiotensin converting enzyme inhibitor. Kits containing such combinations and methods of using such compns. for the treatment of diabetes, diabetes-related disorders, hypertension, and hypertension-related disorders. Example compound I and I+H3PO₄ was prepared by a multistep procedure (procedure given). Compound I and I+H3PO₄ were evaluated for their DPP-4 inhibitory activity.

IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); US&S (Uses)
 (preparation of sitagliptin phosphate and combination of particular DPP-4 inhibitor and antihypertensive agent selected from angiotensin II receptor antagonist and ACE inhibitor for treatment of diabetes and hypertension)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LS ANSWER 25 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2007:201253 CAPLUS Full-text
 DN 146:259149
 TI New crystalline form of perindopril erbiumine
 IN Griesser, Ulrich; Niederwanger, Verena
 PA Sandoz A.-G., Switz.
 SO PCT Int. Appl., 21pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007020009	A1	20070222	WO 2006-EP7923	20060810

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI SI 2005-231 A 20050812
 AB The present invention relates to new crystalline form of the ACE inhibitor perindopril and processes for the preparation thereof. Cryst. form D of perindopril erbiumine is formulated into a pharmaceutically acceptable dosage form, such as a tablet, pill, capsule or injectable for use in the treatment of cardiovascular diseases. Thus, 0.25 g of perindopril erbiumine form A were suspended in 5 mL of dichloromethane and the suspension was heated up to 40°. The clear solution was cooled down to room-temperature at a rate of about 10K/h, filtered under reduced pressure and air-dried to yield 0.23 g (92%) perindopril erbiumine crystalline form D.

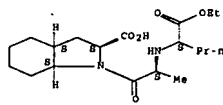
IT 107133-36-8, Perindopril erbiumine
 RL: PRP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (preparation of crystalline form of perindopril erbiumine for dosage forms)

RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
 CMF C4 H11 N



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 26 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2007:200622 CAPLUS Full-text
 DN 146:259148
 TI A process for the preparation of perindopril erbiumine for dosage forms
 IN Ham, Zoran; Furic, Borut
 PA Lek Pharmaceut. D.D., Slovenia
 SO PCT Int. Appl., 26pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007020012	A1	20070222	WO 2006-EP7926	20060810

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI SI 2005-232 A 20050812
 AB The present invention relates to a new process for the preparation of pure perindopril erbiumine. The present invention also relates to a new process for the preparation of crystalline form D of perindopril erbiumine. Crystalline

perindopril erbiumine is formulated into a pharmaceutically acceptable dosage form. Thus, (2S,3aS,7aS)-2-carboxyphenylindole benzyl ester was treated with N-[(S)-1-carboxybutyl]-L-alanine in acetonitrile in presence of O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate to afford 88% perindopril benzyl ester. Hydrogenolysis of crude perindopril benzyl ester over 10% Pd/C gave crude perindopril (2.33% of diketopiperazine I, 0.54% of diketopiperazine II). Crude perindopril was dissolved in wet Et acetate, insol. impurities were filtered off, tert-butylamine was added to the filtrate, the mixture was heated to boiling, filtered and then cooled to 0° to precipitate perindopril erbiumine in crystalline form D.

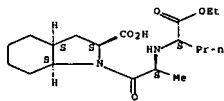
IT 107133-36-8P, Perindopril erbiumine
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of perindopril erbiumine and its crystalline form for dosage forms)

RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
 CMF C4 H11 N

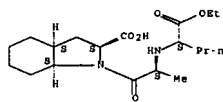


IT 82834-16-0P, Perindopril 122454-52-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of perindopril erbiumine and its crystalline form for dosage forms)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

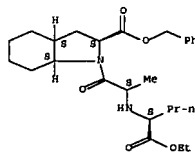
Absolute stereochemistry. Rotation (-).



RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 27 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2007:175534 CAPLUS Full-text
 DN 146:236294
 TI Preparation of novel crystalline η (eta) form of perindopril erbiumine
 IN Ujagare, Ashish; Lochrekar, D. A.; Sarjekar, Pushpalata
 PA Arch Pharmalabs Limited, India
 SO PCT Int. Appl., 21pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007017894	A2	20070215	WO 2006-IN156	20060504
WO 2007017894	A3	20070510		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

UE, OH, OM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

HW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRA1 IN 2005-MU561 A 20050505

AB The present invention relates to a novel crystalline η form of perindopril erbumine exhibiting characteristic 2 θ values and having purity not less than 99.9%. More particularly, the present invention relates to a process for the preparation of the novel crystalline η form of perindopril erbumine comprising the steps of (i) dissolving perindopril erbumine monohydrate in halogenated hydrocarbon solvent; (ii) adding a co-solvent to the mixture of the content obtained from step (i); (iii) removing the mixture of solvents under reduced pressure in the range of 25 to 35°; and (iv) filtering off the solid obtained.

IT 10133-36-AP, Perindopril erbumine

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(preparation and purification of η crystal form of perindopril erbumine of high purity and good solubility)

RN 107133-36-8 CAPLUS

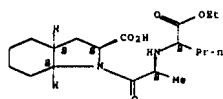
CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1)] (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



IT 690267-97-1P, Perindopril erbumine monohydrate

RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)

(preparation and purification of η crystal form of perindopril erbumine of high purity and good solubility)

RN 690267-97-1 CAPLUS

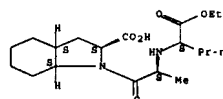
CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



IT 122454-52-8P

RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

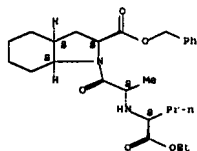
(preparation and purification of η crystal form of perindopril erbumine of high purity and good solubility)

RN 122454-52-8 CAPLUS

CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1:1) (CA INDEX NAME)

(2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



IT 924637-23-0P

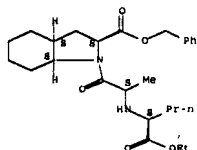
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and purification of η crystal form of perindopril erbumine of high purity and good solubility)

RN 924637-23-0 CAPLUS

CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, phenylmethyl ester, hydrochloride (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

LA English

PAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007017893	A2	20070215	WO 2006-IN155	20060504
WO 2007017893	A3	20070510		

M: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

HW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRA1 IN 2005-MU562 A 20050505

AB The present invention relates to a novel crystalline form of perindopril erbumine monohydrate exhibiting characteristic 2 θ values and having purity not less than 99.9%. More particularly, the present invention relates to a process for the preparation of the novel η form of perindopril erbumine monohydrate comprising steps of (i) dissolving perindopril erbumine in water; (ii) extracting the solution with toluene or xylene; (iii) removing water from the aqueous layer obtained from step (i); adding a polar solvent to the mass obtained from step (ii) at 20 to 45°; and (iv) filtering off the solid obtained.

IT 690267-97-1P, Perindopril erbumine monohydrate

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(preparation and purification of crystalline form of perindopril erbumine monohydrate of high purity)

RN 690267-97-1 CAPLUS

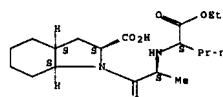
CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



LA AMER 28 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:175533 CAPLUS Full-text

DN 146/236293

TI Preparation of novel crystalline form of perindopril erbumine monohydrate

IN Ujagere, Ashish; Kochhar, D. A.; Sarjekar, Pushpalata

PA Arch Pharm Labs Ltd, India

SO PCT Int. Appl., 21pp.

CODEN: PIXXD2

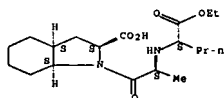
DT Patent

CM 2
 CRN 75-64-9
 CMF C4 H11 N



IT 107133-36-8P, Perindopril erbumine
 RL: PRP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
 (preparation and purification of crystalline form of perindopril erbumine monohydrate of high purity)
 RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)
 CM 1
 CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



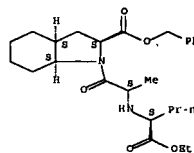
CM 2
 CRN 75-64-9
 CMF C4 H11 N



IT 122454-52-8P
 RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic

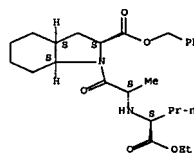
preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and purification of crystalline form of perindopril erbumine monohydrate of high purity)
 RN 122454-52-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



IT 924637-23-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and purification of crystalline form of perindopril erbumine monohydrate of high purity)
 RN 924637-23-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, hydrochloride (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

ANSWER 29 OF 186 CAPLUS COPYRIGHT 2007 ACS on BTN
 2007:174003 CAPLUS Full-text
 146:22608
 TI Process for the preparation of crystalline perindopril

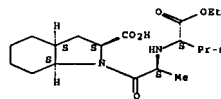
IN Jenko, Branko; Popar, Anton
 PA Lek. Farmaceutična D.D., Slovenia
 SO PCT Int. Appl. 28pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN, CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007017087	A1	20070215	WO 2006-EP7258	20060724
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM PRAI SI 2005-214 A 20050725				

AB The present invention relates to a new process for the preparation of crystalline perindopril. The present invention also relates to new alkyl ammonium salts of perindopril and the processes for the preparation thereof. A pharmaceutical composition comprising a therapeutically effective amount of high pure crystalline perindopril or perindopril alkyl ammonium salts or inclusion complexes of perindopril or perindopril alkyl ammonium salts with cyclodextrins or their alkylated and hydroxyalkylated derivs. are also claimed. Thus, (2S,3aS,7aS)-2-carboxyperhydroindole benzyl ester was treated with N-[(S)-1-carboxybutyl]-(S)-alanine in acetonitrile in presence of O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium to afford perindopril benzyl ester in yield of 88%. Hydrogenolysis of the latter over 10% Pd/C yielded crude perindopril. Crude perindopril obtained was treated with tert-octylamine affording crystalline tert-octylammonium salt of perindopril in yield of 78%. Pure perindopril was precipitated from the crystalline tert-octylammonium salt of perindopril in presence of sulfuric acid and extracted with diisopropyl ether as solid glassy material.

IT 82834-16-0P, Perindopril 924264-24-4P
 924244-25-5P
 RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation and compns. of crystalline perindopril and its alkyl ammonium salts)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

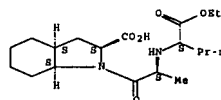
Absolute stereochemistry. Rotation (-).



RN 924264-24-4 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2,2-dimethyl-1-propanamine (1:1) (CA INDEX NAME)

CM 1
 CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



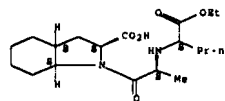
CM 2
 CRN 5813-64-9
 CMF C5 H13 N

H₃C-CH₂-NH₂

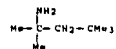
RN 924264-25-5 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2,4,4-trimethyl-2-pentanamine (1:1) (CA INDEX NAME)

CM 1
 CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 107-45-9
CMP C8 H19 N

IT 107133-16-8, Perindopril erbumine

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and compns. of crystalline perindopril and its alkyl ammonium salts)

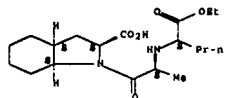
RN 107133-16-8 CAPLUS

CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



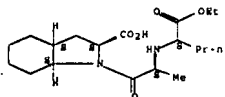
CM 2

CRN 75-64-9
CMP C4 H11 N

RN 82834-16-0 CAPLUS

CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



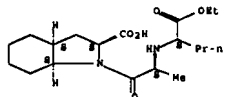
RN 924264-24-4 CAPLUS

CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2,2-dimethyl-1-propanamine (1:1) (CA INDEX NAME)

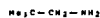
CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 5813-64-9
CMP C5 H13 N

RN 924264-25-5 CAPLUS

CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2,4,4-trimethyl-2-pentanamine (1:1) (CA INDEX NAME)

CM 1



IT 924264-25-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and compns. of crystalline perindopril and its alkyl ammonium salts)

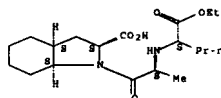
RN 924264-25-3 CAPLUS

CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, benzoate (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 65-85-0
CMP C7 H6 O2

IT 82834-16-0D, Perindopril, inclusion complexes with cyclodextrins

924264-24-0D, inclusion complexes with cyclodextrins

924264-25-0D, inclusion complexes with cyclodextrins

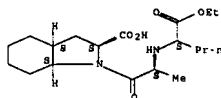
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation and compns. of crystalline perindopril and its alkyl ammonium salts)

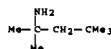
CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 107-45-9
CMP C8 H19 NRE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS NUMBER 30 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2007:150959 CAPLUS Full-text

DN 146:206198

TI Process for the preparation of intermediates of perindopril

IN Joshi, Narendra Shriram; Ramam, Buddharapu Pattabhi; Bodkhe, Arjun

Rajaram

PA Glenmark Pharmaceuticals Limited, India

SO U.S. Pat. Appl. Publ., 7pp.

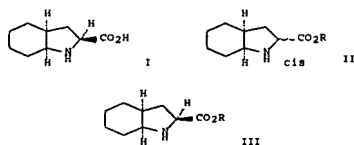
CODEN: USAXCO

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007032661	A1	20070208	US 2006-495102	20060728
IN 2005MU00903	A	20070709	IN 2005-MU903	20050803
PRAT IN 2005-MU903	A	20050803		
US 2005-713000P	P	20050803		
OS CASREACT 146:206198; MARPAT 146:206198				
GI				

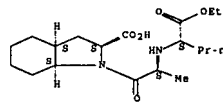


AB A process for the preparation of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid (I) is provided comprising (a) esterifying a cis-perhydroindole-2-carboxylic acid (II) with a first alc. of the formula ROH and a suitable free acid to provide the acid salt I.IAS (Ad = acid), (b) reacting the acid salt with a first base to provide an ester (III), (c) treating the product of step (b) with an L-tartaric containing acid in a second alc. of the formula ROH to precipitate an ester salt III.L-tartarate, (d) reacting the ester salt with a second base to provide an ester III, and (e) hydrolyzing the ester to provide the desired compound I. Thus, cis-perhydroindole-2-carboxylic acid was esterified with benzyl alc. in the presence of p-toluenesulfonic acid under refluxing with azeotropic removal of water to give benzyl perhydroindole-2-carboxylate p-toluenesulfonate which was treated with triethylamine in CH₂Cl₂ to give benzyl cis-perhydroindole-2-carboxylate (IV). A solution of IV with methanol was treated with a solution of dibenzoyl-L-tartaric acid in methanol and the resulting mixture was stirred at 25° for .apprx.30 min., heated at .apprx.60° for .apprx.1 h, and cooled to 15°, followed by filtering the precipitated solid and drying at .apprx.60° to give benzyl (2S,3aS,7aS)-perhydroindole-2-carboxylate L-tartarate (V). V was added to CH₂Cl₂, treated with aqueous NaOH solution, stirred for 1 h to give, after workup, benzyl (2S,3aS,7aS)-perhydroindole-2-carboxylate which was refluxed in a NaOH/aqueous methanol solution for .apprx.2 h, adjusted to pH .apprx.6 to .apprx.7 with dilute aqueous HCl solution, concentrated, treated with ethanol, refluxed, filtered to remove inorg., and concentrated to give I. I was converted into perindopril tert-butylamine salt which is a prodrug for perindoprilat (angiotensin converting enzyme inhibitor) and used to treat hypertension.

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril tert-butylamine salt
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (preparation of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid as intermediate for perindopril)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



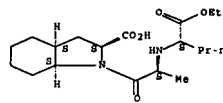
RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



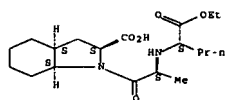
L8 ANSWER 31 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2007:98910 CAPLUS Full-text
 DN 146:434654
 TI Reduction in Arterial Stiffness With Angiotensin II Antagonism and Converting Enzyme Inhibition
 AU Rehman, Asla; Ismail, Shaiful Bahari; Naing, Lin; Roshan, Tariq Mahmood; Rahman, Abdul Rashid Abdul
 CS School of Dental Sciences, Universiti Sains Malaysia, Kelantan, Malay.
 SO American Journal of Hypertension (2007), 20(2), 184-189

CODEN: AJHYE6; ISSN: 0895-7061
 PB Elsevier Inc.
 DT Journal
 LA English

AB Background: Data comparing the effect of losartan and perindopril on aortic stiffness among hypertensive subjects without A1166C polymorphism was not available. Methods: The short-term and long-term effects of losartan (50 mg) and perindopril (4 mg) on aortic stiffness measured as carotid femoral pulse wave velocity (PWV) were compared in 39 middle-aged Malay subjects with mild-to-moderate hypertension in a 4-mo, double-blind, randomized, controlled, parallel-design study. Results: Four-month treatment with both drugs showed a significant reduction in blood pressure (BP) (P < .005) and PWV (P < .05) as compared to the baseline. On the other hand 1-mo treatment showed a significant reduction in BP only in perindopril group (P < .05) but not in the losartan group. There was no significant reduction in pulse pressure and PWV after 1 mo treatment by both drugs. No significant difference was seen in reduction in BP after 1 mo and 4 mo treatment between the two drugs. Similarly no significant difference was seen in reduction in PWV between the two drugs after 1 mo (P = .613) and 4 mo (P = .521) of treatment. Reduction in PWV by losartan (r = 0.470) and perindopril (r = 0.457) correlated significantly only with reduction in DBP (P < .05) and remained significant even after controlling for reduction in DBP (P < .05). Reduction in PWV by both losartan and perindopril was independent of reduction in BP by these drugs. Conclusions: These results showed that long-term treatment with losartan shows similar pressure independent reduction in PWV as perindopril among Malay hypertensive subjects with a homogenous "AA" genotype for angiotensin II type 1 receptor and may serve as a suitable alternative to perindopril.

IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (angiotensin converting enzyme inhibitor perindopril reduced arterial stiffness as was evident by reduction in carotid femoral pulse wave velocity in hypertensive Malay patient without AT1R A1166 polymorphism)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 32 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2007:91096 CAPLUS Full-text
 DN 146:184735
 TI Process for manufacture of (2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-

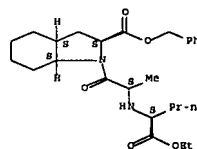
(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (perindopril) and its tert-butyl amine salt
 IN Gunjal, Sanjay Tukaram; Jadhav, Dilip Uttam; Kumar, Ashok; Arpana, Mathur; Panda, Nalinakshya Balaram; Soudagar, Satish Rajanikant
 PA India
 SO U.S. Pat. Appl. Publ., 10 pp., Cont.-in-pat. of U.S. Ser. No. 140,226.
 CODEN: USXXCC
 DT Patent
 LA English
 PAN.CMT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007021490	A1	20070125	US 2006-324349	20060103
IN 2005MU00017	A	20060811	IN 2005-MU17	20050106
US 2006178422	A1	20060810	US 2005-140226	20050527
PRAI IN 2005-MU17	A	20050126		
US 2005-140226	A2	20050527		
IN 2004-MU566	A	20040519		
OS CASREACT 146:184735; MARPAT 146:184735				

AB The invention relates to the preparation of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid), its salts, and its novel intermediates, specifically alkyl ester salts. Thus, (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid was treated with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine in CH₂Cl₂ in the presence of Et₃N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to afford 99% perindopril benzyl ester. Conversion of the latter into the oxalate salt, followed by hydrogenolysis over 5% Pd/C and reaction with tert-butylamine yielded perindopril erbumine.

IT 122454-52-8P 897922-11-1P 897922-12-2P
 897922-13-3P 897922-14-4P 897922-15-5P
 897922-16-6P 897922-18-6P 897922-19-9P
 897922-20-2P 897922-21-3P 897922-22-4P
 897922-23-5P 897922-24-6P 897922-25-7P
 897922-26-9P 897922-27-9P
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (process for synthesis of perindopril, its salts and its alkyl ester salt intermediates)
 RN 122454-52-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



10576386

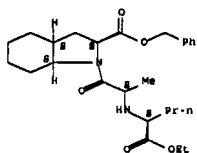
61 of 361

RN 897922-11-1 CAPLUS
 CN Butanedioic acid, 2,3-bis[(4-methylbenzoyloxy)-, (2R,3R)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:7) (CA INDEX NAME)

CM 1

CRN 122454-52-8
 CMF C26 H38 N2 O5

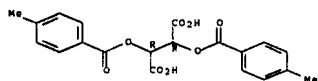
Absolute stereochemistry.



CM 2

CRN 32634-66-5
 CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).



RN 897922-12-2 CAPLUS

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyloxy)-, (2R,3R)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:7) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMF C19 H32 N2 O5

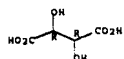
Absolute stereochemistry. Rotation (-).

10576386

63 of 361

CRN 87-69-4
 CMF C4 H6 O6

Absolute stereochemistry.



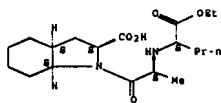
RN 897922-14-4 CAPLUS

CN Butanedioic acid, 2,3-dihydroxy-, (2R,3R)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:7) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMF C19 H32 N2 O5

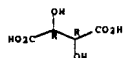
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
 CMF C4 H6 O6

Absolute stereochemistry.



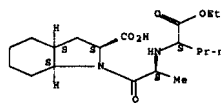
RN 897922-15-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, phosphate (1:7) (CA INDEX NAME)

CM 1

10576386

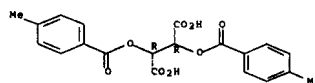
62 of 361



CM 2

CRN 32634-66-5
 CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).



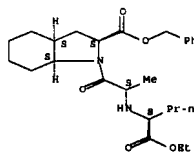
RN 897922-13-3 CAPLUS

CN Butanedioic acid, 2,3-dihydroxy-, (2R,3R)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:7) (CA INDEX NAME)

CM 1

CRN 122454-52-8
 CMF C26 H38 N2 O5

Absolute stereochemistry.



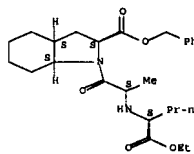
CM 2

10576386

64 of 361

CRN 122454-52-8
 CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

CRN 7664-38-2
 CMF H3 O4 P



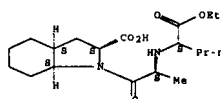
RN 897922-16-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, phosphate (1:7) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

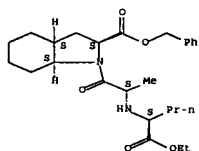
CRN 7664-38-2
CMF H3 O4 P

RN 897922-18-8 CAPLUS
CN 1,2-Benzenedicarboxylic acid, compd. with phenylmethyl
(2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:7) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

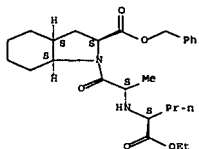
Absolute stereochemistry.



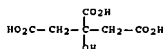
CM 2

CRN 88-99-3
CMF C8 H6 O4

RN 897922-19-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, (1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonate (1:7) (CA INDEX NAME)



CM 2

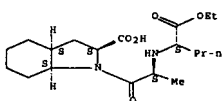
CRN 77-92-9
CMF C6 H8 O7

RN 897922-21-3 CAPLUS
CN 1,2-Benzenedicarboxylic acid, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:7) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



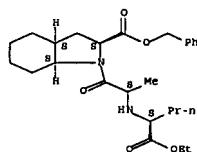
CM 2

CRN 88-99-3
CMF C8 H6 O4

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

CRN 3144-16-9
CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (+).



RN 897922-20-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:7) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

Absolute stereochemistry.

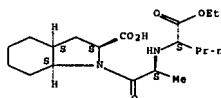


RN 897922-22-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, (1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonate (1:7) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 3144-16-9
CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (+).

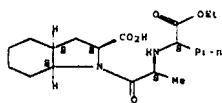


RN 897922-23-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:7) (CA INDEX NAME)

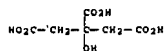
CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 77-92-9
CMP C6 H8 O7

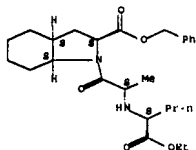
RN 897922-24-6 CAPLUS

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyloxy)-, (2S,3S)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:7) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMP C26 H38 N2 O5

Absolute stereochemistry.



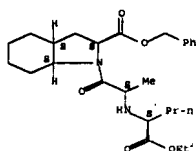
CM 2

1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:7) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMP C26 H38 N2 O5

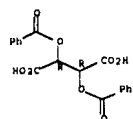
Absolute stereochemistry.



CM 2

CRN 22333-70-6
CMP C18 H14 O8

Relative stereochemistry.



RN 897922-27-9 CAPLUS

CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2R,3R)-rel-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:7) (CA INDEX NAME)

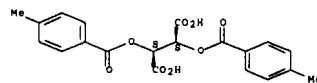
CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CRN 32634-68-7
CMP C20 H18 O8

Absolute stereochemistry. Rotation (+).



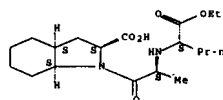
RN 897922-25-7 CAPLUS

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyloxy)-, (2S,3S)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:7) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

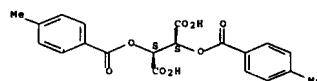
Absolute stereochemistry. Rotation (-).



CM 2

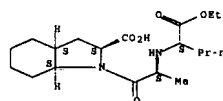
CRN 32634-68-7
CMP C20 H18 O8

Absolute stereochemistry. Rotation (+).



RN 897922-26-8 CAPLUS

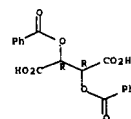
CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2R,3R)-rel-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:7) (CA INDEX NAME)



CM 2

CRN 22333-70-6
CMP C18 H14 O8

Relative stereochemistry.



IT 107133-36-3P, Perindopril erbumine

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (process for synthesis of perindopril, its salts and its alkyl ester salt intermediates)

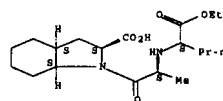
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

IT 897922-09-7 897922-10-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(process for synthesis of perindopril, its salts and its aralkyl ester salt intermediates)

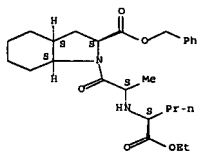
RN 897922-09-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, ethanedioate (1:1) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

CRN 144-62-7
CMF C2 H2 O4

RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI IN 2005-DE1694 A 20050630

OS CASREACT 146:122305

AB An improved process for the preparation of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] comprises treating silylated (2S,3aS,7aS)-2-carboxyhydroindole with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanyl chloride hydrochloride. In an example, silylation of (2S,3aS,7aS)-2-carboxyhydroindole was carried using hexamethyldisilazane and imidazole in methylene chloride. Crude perindopril was converted to perindopril tert-butylamine salt.

IT 82834-16-0P, Perindopril 107133-36-0P, Perindopril erbumine

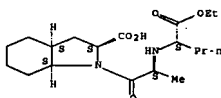
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of perindopril by acylation of silylated carboxyhydroindole)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



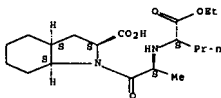
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



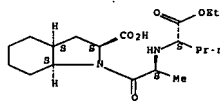
RN 897922-10-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, ethanedioate (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 144-62-7
CMF C2 H2 O4

ANSWER 33 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007-33054 CAPLUS Full-text

DN 146:122305

TI Process for the preparation of perindopril

IN Nath, Asok; Piyasid, Mohan

PA Ranbaxy Laboratories Limited, India

SO PCT Int. Appl., 17pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007004165	A2	20070111	WO 2006-IB52191	20060629
WO 2007004165	A3	20070322		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GN, GR, GU, HT, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				

CM 2

CRN 75-64-9
CMF C4 H11 N

ANSWER 34 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006-1354230 CAPLUS Full-text

DN 146:100711

TI Thienopyrimidines for pharmaceutical compositions and their preparation

IN Jaekel, Stefan; Murfin, Stefan; Taylor, Steven; Aicher, Babette; Kelter, Arnd-Rene; Colter, Thomas Stefan

PA Develogen Aktiengesellschaft, Germany

SO PCT Int. Appl., 180pp.

CODEN: PIXXD2

DT Patent

LA English

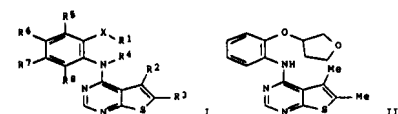
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006136402	A1	20061228	WO 2006-EP5980	20060621
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GN, GR, GU, HT, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI EP 2005-13500

OS MARPAT 146:100711

GI



AB The invention relates to pharmaceutical compds. of formula I comprising thienopyrimidine compds. Compound of formula I wherein X is O, S, SO₂, CH₂, CO, NH and derivs., etc.; R₁ - R₃ are independently H, C1-6 alkyl, C1-6 alkyl-C3-10 (heterocycloalkyl, C3-10 cycloalkyl, C6-10 aryl, etc.); R₄ is H, C1-4 alkyl, (thio)urea, (un)substituted acetyl, 5- to 6-members heterocycle; R₅ - R₇ are independently H halo, CN, CO₂H and derivs., OH and derivs., CONH₂ and derivs., SO₂NH₂ and derivs. etc.; and their metabolites, prodrugs and pharmaceutically acceptable salts thereof, are claimed. Moreover, the present invention relates to the use of the thienopyrimidine compds. of the invention for the production of pharmaceutical compds. for the prophylaxis and/or treatment of diseases which can be influenced by the inhibition of the kinase activity of Mnk1 and/or Mnk2 (Mnk2a or Mnk2b) and/or variants thereof. Example compound II was prepared by substitution of 2-fluoronitrobenzene with 3-hydroxytetrahydrofuran; the resulting 3-(2-nitrophenoxy)tetrahydrofuran underwent hydrogenation to give 3-(2-aminophenoxy)tetrahydrofuran, which underwent arylation with 4-chloro-5,6-dimethylthieno[2,3-d]pyrimidine. All the invention compds. were evaluated for their kinase inhibitory activity.

IT 82834-16-0, Perindopril

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

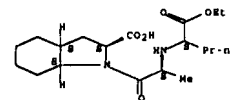
(Biological study); USSES (Uses)

(preparation of thienopyrimidine compds. useful in prophylaxis and treatment of diseases)

RN 82834-16-0 CAPLUS

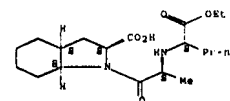
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 36 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM 2006:1353979 CAPLUS Full_text



CM 2

CRN 75-64-9
CMP C4 H11 N



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 36 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM 2006:1353979 CAPLUS Full_text

DN 146:45750

TI Process for the preparation of perindopril

IN Sinha, Brajesh Kumar; Vardil, Pandu Ranga Rao; Budidet, Shankar Reddy;

Dandala, Ramesh; Moenakia; Sivakumaran, Sivakumaran

PA Aurbindo Pharma Limited, India

SO PCT Int. Appl., 16pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006:131828	A1	20061214	WO 2006-181583	20060601
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GO, GM, ML, MR, NE, SN, TD, TG, BW, GH, OM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
IN 2005CH00703	A	20070727	IN 2005-CH703	20050608
IN 2005CH01355	A	20070928	IN 2005-CH1355	20050926
PRAI IN 2005-CH703	A	20050608		

DN 146:101038

TI Process for industrially-viable preparation of perindopril erbumine

IN Potluri, Ramesh Babu; Venkata Subramanian, Hariharakrishnan; Mulakala,

Atchuta Ramayya Chowdary; Kodali, Hari Prasad

PA India

SO PCT Int. Appl., 17pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006:137082	A1	20061228	WO 2006-IN182	20060629
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GO, GM, ML, MR, NE, SN, TD, TG, BW, GH, OM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
IN 2005CH00783	A	20070727	IN 2005-CH783	20050623
PRAI IN 2005-CH783	A	20050623		
OS CASREACT 146:101038; MARPAT 146:101038				
AB A novel method for the preparation of perindopril erbumine [(2S,3aS,7aS)-1-[(S)-1-(ethoxycarbonyl)butyl]-L-alanyl]octahydro-1H-indole-2-carboxylic acid tert-butylamine salt] comprises treating (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid (I) esters with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine, followed by deprotection and conversion to the erbumine salt. 1 benzyl ester hydrochloride was prepared from hexahydroindoline-2-carboxylic acid hydrochloride by catalytic hydrogenation, followed by esterification and resolution with dibenzoyl-L-tartaric acid or benzyloxycarbonyl-L-phenylalanine.				
IT 107133-36-9P, Perindopril erbumine				
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)				
(preparation of perindopril erbumine)				
RN 107133-36-8 CAPLUS				
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)				
CM 1				
CRN 82834-16-0				
CMP C19 H32 N2 O5				

Absolute stereochemistry. Rotation (-).

IN 2005-CH1355

OS CASREACT 146:45750; MARPAT 146:45750

AB An improved process for the preparation of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] comprises treating (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid benzyl ester p-toluenesulfonic acid salt with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine [e.g., in MeCN in the presence of 4-(dimethylamino)pyridine], followed by hydrogenolysis of perindopril benzyl ester over 5% Pd/C.

IT 82834-16-0P, Perindopril

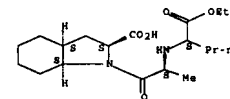
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 107133-36-9P, Perindopril erbumine

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of perindopril)

RN 107133-36-8 CAPLUS

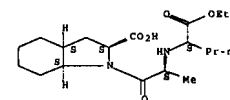
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



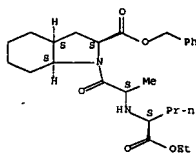
10576386
CM 2
CRN 75-64-9
CMF C4 H11 N

81 of 361



IT 122454-52-8F
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of perindopril)
RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

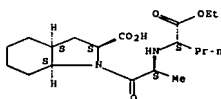
Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 37 OF 166 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1252442 CAPLUS Full-text
DN 146:27826
TI Preparation of pyrazole compounds as hepatic glycogen phosphorylase inhibitors and therapeutic agents for diabetes
IN Takagi, Masaki; Nakamura, Takeshi; Matsuda, Isamu; Fukuda, Kenji; Ozawa, Koichi; Ueda, Nobuhisa; Sakata, Kaoru; Nomura, Yukihiro
PA Japan Tobacco Inc., Japan
SO PCT Int. Appl., 490pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2006126695 A1 20061130 WO 2006-JP310603 20060522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

10576386 83 of 361
Absolute stereochemistry. Rotation (-).



CM 2
CRN 75-64-9
CMF C4 H11 N



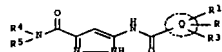
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 38 OF 166 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1226928 CAPLUS Full-text
DN 145:505259
TI Preparation of 4-biaryl-1-phenylazetidin-2-ones for the treatment of hypercholesterolemia
IN Antonelli, Stephen; Barden, Timothy C.; Cali, Brian; Currie, Mark G.; Lundrigan-Soucy, Regina; Yang, Jing-Jing; Yorgey, Peter S.; Zimmer, Daniel P.; Martinez, Eduardo; Schairer, Wayne C.; Talley, John J.
PA Microbia, Inc., USA
SO PCT Int. Appl., 449pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2006124713 A2 20061123 WO 2006-US18616 20060515
WO 2006124713 A3 20070118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CO, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,

10576386

82 of 361

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CO, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, LM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
JP 2007191461 A 20070802 JP 2006-141015 20060522
US 2007032529 A1 20070208 US 2006-438489 20060523
PRAI JP 2005-148847 A 20050923
US 2005-685037P P 20050526
JP 2005-367286 A 20051220
US 2006-755820P P 20060103
OS MARPAT 146:27826
OI



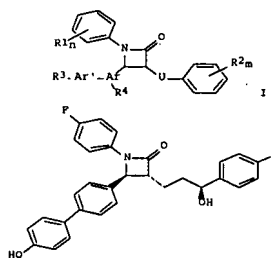
AB The title compds. (I) or pharmacol. acceptable salts thereof [ring Q = aryl or aromatic heterocyclic group; R1 = H, halo, C1-6 alkyl, C1-6 alkoxy; R2 = halo, C1-6 alkyl, C1-6 alkoxy, azido, R3 = halo, hydroxyl, C1-6 alkyl, halo-C1-6 alkyl, C1-6 alkoxy, azido, amino, acylamino, C1-6 alkylsulfonamino; R4, R5 independently = H, C2-6 alkenyl, C2-6 alkynyl, (un)substituted C1-6 alkyl, C3-8 cycloalkyl, C3-8 cycloalkyl-C1-6 alkyl, 5- or 6-membered saturated monocyclic heterocyclic group, aryl, C7-14 C7-14 aralkyl, or 5- or 6-membered aromatic monocyclic heterocyclic group optionally fused to a benzene ring, etc.] are prepared. These compds. have a hepatic glycogen phosphorylase inhibitory activity and therefore is useful as a therapeutic or prophylactic agent for diabetes. Thus, 6.00 g 5-(2-chloro-4,5-difluoro-benzoylamino)-1H-pyrazole-3-carboxylic acid imidazole was suspended in 50 mL DMF, treated with 1.72 mL 3-picolyamine under ice-cooling, and stirred at room temperature overnight to give 4.49 g 5-(2-chloro-4,5-difluoro-benzoylamino)-1H-pyrazole-3-carboxylic acid N-(pyridin-3-ylmethyl)amide (II). II showed IC50 of <100 nM against human hepatic glycogen phosphorylase.
IT 107133-36-3, Perindopril Erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preparation of pyrazole compds. as hepatic glycogen phosphorylase inhibitors and therapeutic agents for diabetes)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1
CRN 82834-16-0
CMF C19 H32 N2 O5

10576386

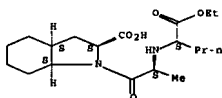
84 of 361

GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRAI US 2005-681232P P 20050513
US 2005-695988P P 20050701
OS MARPAT 145:505259
OI



AB 4-Biaryl-1-phenylazetidin-2-ones of formula I [R1-R4 = H, halo OH, alkyl, alkoxy, CN, etc.; R5 = alkylene, etc.; Ar = aryl, heteroaryl; Ar' = aryl] are prepared which are useful for the treatment of hypercholesterolemia. Thus, II was prepared, and had ED50 value of 0.002 mg/kg in rat cholesterol absorption model.
IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (co-drug; preparation of biarylphenylazetidinones for treatment of hypercholesterolemia)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LA ANSWER 39 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2006:1177333 CAPLUS Full-text
 DN 145:465604
 TI Combination of a HMG-CoA reductase inhibitor and a drug intervening in the renin-angiotensin system for treating respiratory disorders
 IN Lindmark, Bertil; Thoren, Anders; Higenbottam, Timothy William
 PA Astrazeneca AB, Sued.; Astrazeneca UK Limited
 SO PCT Int. Appl., 31pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006117534	A2	20061109	WO 2006-GB1582	20060428
WO 2006117534	A3	20070125		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

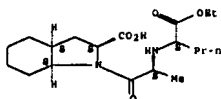
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GQ, GM, ML, MR, NE, SN, TD, TG, BW, GH, OM, KE, LA, MM, ME, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI GB 2005-8924 A 20050430
 AB The invention provides medicaments comprising a combination of a HMG-CoA reductase inhibitor and a drug intervening in the renin-angiotensin system selected from angiotensin II antagonists and angiotensin converting enzyme (ACE) inhibitors optionally in combination with a bronchodilator and a glucocorticosteroid in the treatment of respiratory disorders such as chronic obstructive pulmonary disease (COPD).

IT 2005-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (combination of a HMG-CoA reductase inhibitor and a drug intervening in the renin-angiotensin system for treating respiratory disorders)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

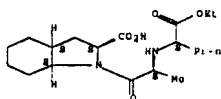


hydroxypentanoil]oxazolidinone. Examples demonstrating hypolipemic and anticholesteremic activity of I and similar compds. were given, e.g., using the rat cholesterol absorption model.

IT 82834-16-0, Perindopril
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (biaryl(phenyl)azetidione glucuronide derivs. preparation for hypercholesterolemia)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LA ANSWER 41 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2006:117967 CAPLUS Full-text
 DN 145:418947
 TI Preparation of α -form crystals of perindopril erbumine
 IN Tanbe, Kiyoyuki; Imai, Eiji
 PA Shiono Chemical Co., Ltd., Japan
 SO Jpn. Kokai Tokyo Koho, Spp.
 CODEN: JKKXAP
 DT Patent
 LA Japanese
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2006290825	A	20061026	JP 2005-115676	20050413
PRAI JP 2005-115676		20050413		

AB α -form crystals of antihypertensive perindopril erbumine (α -I) is prepared by dissolving crude crystals of I in solvents and rapidly cooling the solution to a temperature lower than room temperature in the presence of seed crystals of α -I. Thus, crude crystals of 17.2 g I was dissolved in EtOAc upon heating to 78°, seed crystals were added, and the solution was cooled with an ice water to 4° over 10 min to give 13.0 g α -I.

IT 107133-36-8, Perindopril erbumine
 RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PVP (Physical process); PREP (Preparation); PROC (Process)

(preparation of α -form crystals of perindopril erbumine by dissolving crude crystals in solvents and rapidly cooling the solution in the presence of seed crystals)

RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-

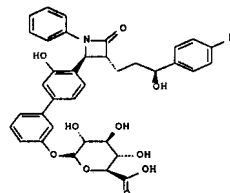
LA ANSWER 40 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2006:115934 CAPLUS Full-text
 DN 145:465730
 TI 4-Biaryl-1-phenylazetid-2-one glucuronide derivatives for hypercholesterolemia
 IN Lundigran-Soucy Regina
 PA Microbia, Inc. USA; Martinez, Eduardo; Talley, John J.
 SO PCT Int. Appl., 20pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006116499	A1	20061102	WO 2006-US15814	20060426

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GQ, GM, ML, MR, NE, SN, TD, TG, BW, GH, OM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-674729P P 20050426
 OS CASREACT 145:465730; MARPAT 145:465730
 GI

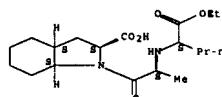


AB The invention relates to a chemical genus of 4-biaryl-1-phenylazetid-2-ones useful for the treatment of hypercholesterolemia and other disorders. E.g., I was prepared starting from 5-benzyl-1-[5-(4-fluorophenyl)-5-

(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1
 CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2
 CRN 75-64-9
 CMF C4 H11 N



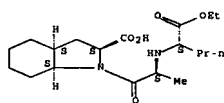
LA ANSWER 42 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2006:1097392 CAPLUS Full-text
 DN 145:426033
 TI Aerosol composition comprising non-ionic surfactant and phospholipid
 IN Keller, Manfred; Friedrich, Ingo; Jauernig, Juergen; Lintz, Frank-Christophe
 PA Pari O.G.m.b.H. Spezialisten fuer Effekte Inhalation, Germany
 SO PCT Int. Appl., 72pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006108556	A2	20061019	WO 2006-EP3147	20060406
WO 2006108556	A3	20070503		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

VN, YU, ZA, ZM, ZW
 RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
 EP 1712220 A1 20061018 EP 2005-8322 20050415
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU
 PRAI EP 2005-8322 A 20050415
 AB Sterile compns. for administration as aerosols are described. They contain an active agent which is poorly water-soluble, a non-ionic surfactant component and a phospholipid component. The compns. are suitable for oral or nasal inhalation, but also for topical or mucosal administration. They are particularly useful for the efficient pulmonary administration of poorly soluble corticosteroids and can be aerosolized with common nebulizers. For example, tyloxapol 2 g, DMPC 2 g, and tocopherol acetate 20 mg were mixed with water 200 mL for injection and pre-homogenized with an Ultra Turrax. The dispersion was homogenized for about 15 min in a high-pressure homogenizer at 1500 bar. Reduced glutathione 2.5 g were rapidly dissolved in 50 mL of the resulting colloidal solution with stirring and the pH was adjusted to 6 by addition of lysine monohydrate. The resulting colloidal glutathione-vitamin E acetate solution was immediately sterile filtered into glass vials and subsequently freeze dried.
 IT 82834-16-0, Perindopril
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical aerosol composition comprising non-ionic surfactant and phospholipid)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

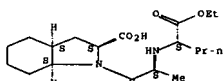
Absolute stereochemistry. Rotation (-).



ANSWER 43 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2006:1039848 CAPLUS Full-text
 DN 145:397363
 TI Process for the synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its esters, useful intermediates in the manufacture of perindopril, via resolution of 2,3-dihydroindole-2-carboxylic acid alkyl esters and catalytic hydrogenation of (2S)-2,3-dihydroindole-2-carboxylic acid
 IN Le, Goffic, Francois
 PA Laboratoire Substipharm, Fr.
 SO Fr. Demande, 20pp.
 CODEN: FRXXBL

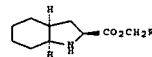
ANSWER 44 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2006:983574 CAPLUS Full-text
 DN 146:93014
 TI Arterial hypertension: oxidative stress and endothelial dysfunction
 AU Vaskina, E.; Demin, A.; Tayrendorjiev, D.; Pustovetova, M.
 CS Novosibirsk State Medical Academy, Novosibirsk, 630091, Russia
 SO Proceedings - KORUS 2004, Korea-Russia International Symposium on Science and Technology, 8th, Tomsk, Russian Federation, June 26-July 3, 2004 (2004), Volume 3, 361-363 Publisher: Institute of Electrical and Electronics Engineers, New York, N. Y.
 CODEN: 691LJH; ISBN: 0-7803-8383-4
 DT Conference
 LA English
 AB The aim of the study was to investigate the pathogenetic significance of oxidative stress (OS) in the development of endothelial vascular dysfunction (EO) in essential arterial hypertension (AH) and to determine the possibilities of the markers usage for evaluation of antihypertensive drugs influence on leukocyte-endothelial interaction (LEI). Methods of research included evaluation of OS, approx. oxidative metabolism of polymorphonuclear leukocytes (PML) by chemiluminescence (ChL), proinflammatory cytokines (interleukin-1 β , TNF- α) by immunoenzyme methods, and ED, including evaluation of nitric oxide (NO) and hemostasis procoagulant factors. Results. It was revealed increased OS and ED in AH. In the frames of 4-wk randomized controlled clin. trial AT II receptors antagonist valsartan and ACE inhibitor perindopril, contrary to beta-adrenergic blocking agent atenolol, except achievement of target arterial pressure, normalize or considerably lower the raised oxidative stress and endothelial dysfunction, including proinflammatory cytokines and procoagulant factors activity, at arterial hypertension of 2-3 severity degrees with further delay of pathol. process progressing in patients. Conclusion. This investigation proves that the OS has important pathogenetic value for ED development at AH when arising damages of LEI conduct to proinflammation, vasoconstriction, prothrombosis, vascular remodeling and to defeat organs-targets.
 IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (marker study show oxidative stress in endothelial vascular dysfunction in growth of arterial hypertension patient with LEI damage led to proinflammation, vasoconstriction, prothrombosis, vascular remodeling, organ-target defeat)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

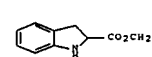


DT Patent
 LA French
 FAN. CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 2883874	A1	20061006	FR 2005-3293	20050404
PRAI FR 2005-3293		20050404		
OS CASREACT 145:397363; MARPAT 145:397363				
GI				



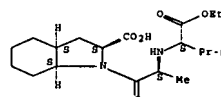
II



III

AB The invention is related to a process for preparation of (-)-(2S,3aS,7aS)-perhydroindole-2-carboxylic acid (I) and its esters II (R = H, alkyl), useful intermediates in the synthesis of perindopril, by (a) enzymic resolution of rac-III (R1 = (un)substituted H, alk(en)yl) by protease-catalyzed hydrolysis to isolate the ester (S)-III and (2R)-2,3-dihydroindole-2-carboxylic acid; (b)aponification or hydrolysis of the ester (S)-III to give (2S)-2,3-dihydroindole-2-carboxylic acid (IV); (c) catalytic hydrogenation of acid IV to give I; (d) isolation of acid I; (e) optionally, esterification of I to give esters of formula II; and (f) isolation of esters II. Advantages include selective preparation of diastereomer acid I in good yield and excellent purity, and simple purification. Thus, acid I was prepared, in > 99% enantiomeric purity, via subtilisin-catalyzed resolution of a mixture of Me 2,3-dihydroindole-2-carboxylate and Et 2,3-dihydroindole-2-carboxylate and hydrogenation of acid IV over Rh/C.
 IT 82834-16-0, Perindopril
 RL: PHU (Preparation, unclassified)
 (synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its esters as useful intermediates in the synthesis of perindopril)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

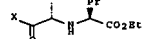
Absolute stereochemistry. Rotation (-).



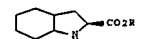
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 45 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2006:980040 CAPLUS Full-text
 DN 145:357099
 TI Process for the preparation of perindopril from ethoxycarbonylbutyl alanyl halide and carboxyperhydroindole
 IN Joshi, Narendra Shriram; Bhirud, Shekhar Bheskar; Rao, Kodali Eswara; Ramam, Buddhavarapu Pattabhi; Soni, Vijay
 PA Glenmark Pharmaceuticals Limited, India
 SO U.S. Pat. Appl. Publ., 6pp.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN. CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006211867	A1	20060921	US 2006-386011	20060321
US 7291745	B2	20071106		
IN 2005MU0306	A	20070609	IN 2005-MU306	20050321
PRAI IN 2005-MU306	A	20050321		
US 2005-666354P	P	20060630		
OS CASREACT 145:357099; MARPAT 145:357099				
GI				



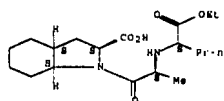
I



II

AB A process for preparing perindopril comprises condensing N-[(S)-1-ethoxycarbonylbutyl]-(S)-alanyl halides (I; X = halo) with (2S,3aS,7aS)-2-carboxyperhydroindoles (II; R = H, protecting group). Thus, N-[(S)-1-ethoxycarbonylbutyl]-(S)-alanyl chloride hydrochloride (preparation given) in CH2Cl2 at -5° was treated with indazole and then with (2S,3aS,7aS)-2-carboxyperhydroindole followed by stirring at -5° for 2 h and at 20-25° for 2 h. Aqueous HCl was added at -5° followed by stirring for 30 min. and separation and drying of the CH2Cl2 layer. This was treated with tert-butylamine at <10° followed by stirring at 35-40°. Distillation of CH2Cl2, addition of Me2CHOH, acetone, and MeCN, heating to 65-70°, and slow cooling to 5-10° to give perindopril erbumine of >99.5% purity.
 IT 82834-16-0P, Perindopril
 RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of perindopril from ethoxycarbonylbutyl alanyl halide and carboxyperhydroindole)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 107133-36-4P, Perindopril erbumine

RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of perindopril from ethoxycarbonylbutyl alanyl halide and carboxyphenylindole)

RN 107133-36-8 CAPLUS

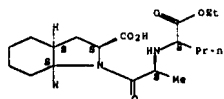
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



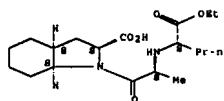
CM 2

CRN 75-64-9

CMP C4 H11 N



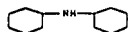
✓ ANSWER 46 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 A 2006:977829 CAPLUS Full-text
 DN 145:342248
 TI An improved process for the purification of perindopril



CM 2

CRN 101-93-7

CMP C12 H23 N



IT 107133-36-4P

RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(Improved process for purification of perindopril)

RN 107133-36-8 CAPLUS

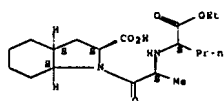
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N

IN Singh, Girdi Pal; Godhole, Himanshu Madhav; Rananaware, Umesh Babanrao; Dumbre, Vilas Nathu; Kambe, Suhas Ganpat; Nehate, Sagar Purushottam

PA Lupin Limited, India

PG 2006:977829 CAPLUS Full-text

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2006097941 A1 20060921 WO 2005-IN189 20050609

W: AS, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NG, NI, NO, NZ, OM, OS, PA, PE, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO, BM, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KO, KZ, MD, RU, TJ, TM

IN 2005MU00275 A 20070525 IN 2005-MU275 20050314

AU 2005329237 A1 20060921 AU 2005-329237 20050609

IN 2007MN01634 A 20071116 IN 2007-MN1634 20071008

PRAI IN 2005-MU275 A 20050314

WO 2005-IN189 M 20050609

AB The present invention relates to perindopril in the form of a salt with dicyclohexylamine, a process for its production and its use in the purification of a impure perindopril. The present invention also relates to preparation of perindopril tert-butylamine salt directly from perindopril dicyclohexylamine salt without isolating the free base. For example, perindopril 25 g was taken in acetonitrile 150 mL and stirred for about 10 min. The above solution was treated with dicyclohexylamine 5.2 g and stirred for about 8-10 h at room temperature. The precipitated solid was filtered and washed with acetonitrile 20 mL. The dicyclohexylamine salt of perindopril 12 g was recrystd. in acetonitrile.

IT 909775-66-5P

RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(Improved process for purification of perindopril)

RN 909776-66-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with N-cyclohexylcyclohexanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

✓ ANSWER 47 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

A 2006:821424 CAPLUS Full-text

DN 145:225771

TI Genetic markers in the HLA-C gene associated with an adverse hematological response to drugs

IN Athanasiou, Maria; Gerson, Stanton

PA US

SO U.S. Pat. Appl. Publ., 25pp.

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 2006183146 A1 20060817 US 2006-351601 20060210

PRAI US 2005-652135P P 20060211

AB Genetic markers in the HLA-C gene associated with adverse hematol. response to drug therapy are disclosed. Comps. and methods for detecting and using these HLA-C markers in a variety of clin. applications are disclosed. Such applications include methods for testing an individual for susceptibility for an adverse hematol. response, methods of selecting the appropriate drug therapy for patients based on the presence or absence of a HLA-C marker, and products comprising a drug with hematol. toxicity that are approved for treating patients lacking a genetic marker.

IT 107133-36-8, Perindopril erbumine

RL: BSU (Biological study, unclassified); BUU (Biological use).

10576386

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unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (method and genetic markers based on HLA-C gene polymorphism for predicting susceptibility to adverse hematol. response to drugs)

RN 107133-36-8 CAPLUS

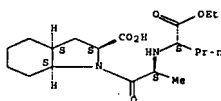
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N



ANSWER 48 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

2006:796623 CAPLUS Full-text

DN 145:230528

TI Process for making highly pure perindopril erbumine

IN Kumar, Ashok; Soudager, Satish Rajanikant; Mathur, Arpana; Shah, Chirag; Hasmukh; Gunjal, Sanjay Tukaram; Metil, Dattatray Shamrao; Kelkar, Rahul; Suresh; Thakare, Devendra Digambar; Kumar, Bindu Manoj; Nair, Raji

PA USA

SO U.S. Pat. Appl. Publ., 6 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006178022	A1	20060810	US 2005-140226	20050527
IN 2004MU00566	A	20060616	IN 2004-MU566	20040518

10576386

99 of 361

IT 107133-36-5P, Perindopril erbumine

RL: SPN (Synthetic preparation); PREP (Preparation) (process for making highly pure perindopril erbumine)

RN 107133-36-8 CAPLUS

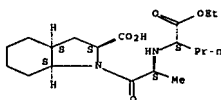
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N



ANSWER 49 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

2006:796580 CAPLUS Full-text

DN 145:224831

TI Genetic markers in the HLA-DQB1 gene associated with an adverse hematological response to drugs, and genotyping for drug risk assessment

IN Athanasiou, Maria; Gerson, Stanton

PA USA

SO U.S. Pat. Appl. Publ., 30pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006177860	A1	20060810	US 2006-351394	20060209
PRAI US 2005-651835P	P	20050209		

10576386

98 of 361

US 2007021490 A1 20070125 US 2006-324349 20060103

PRAI IN 2004-MU566 A 20040506

IN 2005-MU17 A 20050106

US 2005-140226 A2 20050527

OS CASREACT 145:230528

AB A process for the synthesis and isolation of (2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid and its tert-butylamine salt, comprises the amidation of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester and N-[(S)-1-carboxybutyl]- (S)-alanine Et ester in nonreactive solvents in turn avoiding the formation of the impurity N-acetyl (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester. The de-protection of benzyl ester group is optimized by catalytic hydrogenolysis and then isolation of the product from an aqueous layer by extraction using an organic solvent, which eliminates the need for lyophilization. This yields perindopril erbumine free of contaminants derivable from dicyclohexylcarbodiimide (e.g., dicyclohexylurea) and impurities originated by the use of Et acetate.

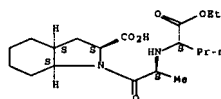
IT 82834-16-0P, Perindopril 122454-52-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (in a process for making highly pure perindopril erbumine)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

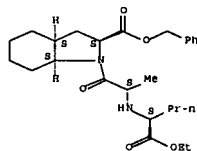
Absolute stereochemistry. Rotation (-).



RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



10576386

100 of 361

AB Genetic markers in the HLA-DQB1 gene associated with adverse hematol. response to drug therapy are disclosed. Comps. and methods for detecting and using these HLA-DQB1 markers in a variety of clin. applications are disclosed. Such applications include methods for testing an individual for susceptibility for an adverse hematol. response, methods of selecting the appropriate drug therapy for patients based on the presence or absence of a HLA-DQB1 marker, and products comprising a drug with hematol. toxicity that are approved for treating patients lacking a genetic marker.

IT 107133-36-8, Perindopril erbumine

RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (genetic markers in HLA-DQB1 gene associated with adverse hematol. response to drugs, and genotyping for drug risk assessment)

RN 107133-36-8 CAPLUS

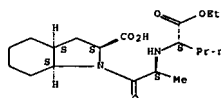
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N



ANSWER 50 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

2006:796329 CAPLUS Full-text

DN 145:224864

TI Hydroxylated nebirolol metabolites for treating and/or preventing vascular diseases

IN O'Donnell, John E.; Owens, Walter; Duncan, Joseph; Shaw, Andrew; Wu, Jinn

PA Mylan Laboratories, Inc., USA

10576386

101 of 361

80 PCT Int. Appl., 120pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006083779	A2	20060810	WO 2006-US3252	20060130
WO 2006083779	A3	20061123		
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, ME, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PA, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SN, SY, TJ, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006210952	A1	20060810	AU 2006-210952	20060130
CA 2596426	A1	20060810	CA 2006-2596426	20060130
US 2007014733	A1	20070118	US 2006-342497	20060130
EP 1848424	A2	20070331	EP 2006-719896	20060130
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI US 2005-648551P	P	20050131		
US 2006-755856P	P	20060103		
WO 2006-US3252	M	20060130		

AB Hydroxylated nebivolol metabolites increase NO release from human endothelial cell preps. in a concentration dependent fashion following acute administration. In addition, hydroxylated nebivolol metabolites, including but not limited to 4-hydroxy-6,6'-difluoro-, 4-hydroxy-5-phenyl-6,6'-difluoro-, and 4-hydroxy-8-phenyl-6,6'-difluoro-, have the ability to increase the capacity for NO release in human endothelial cells following chronic administration. This invention provides hydroxylated nebivolol metabolites and comprs. comprising nebivolol and/or at least one hydroxylated metabolite of nebivolol and/or at least one addnl. compound used to treat cardiovascular diseases or a pharmaceutically acceptable salt thereof. In addition, this invention provides methods of treating and/or preventing vascular diseases by administering at least one hydroxylated metabolite of nebivolol that is capable of releasing a therapeutically effective amount of nitric oxide to a targeted site affected by the vascular disease. Also, this invention is directed to the treatment and/or prevention of migraine headaches by administering at least one hydroxylated metabolite of nebivolol. This invention may also be used in conjunction with or as a single treatment of metabolic syndrome disorders. Thus, acute treatment with six stereoselective hydroxy metabolites in endothelial cells from both white and black American donors showed that all six hydroxy metabolites have activity that was much superior to d-nebivolol, and most are superior to nebivolol racemate. As compared to nebivolol, the 4'-((R)-hydroxy-7-fluoro-6-hydroxy-1-nebivolol metabolite caused a nearly two-fold increase in NO release to 475 ± 20 and 383 ± 18 nmol/L, resp., from white and black donors. The 4'-((R)-hydroxy-5-fluoro-1-nebivolol metabolite also exceeded the activity of nebivolol and even 1-nebivolol by 50%. These findings indicate that hydroxy metabolites of nebivolol have distinct and highly reproducible effects on acute NO release in human endothelial cells.

IT 22214-16-N, Perindopril
 RL: THU (Therapeutic use); BIOL (Biological study); US88 (Uses)

10576386

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AB Genetic markers associated with adverse hematol. response to drug therapy are disclosed in the CSF2RB gene encoding B-chain of colony-stimulating factor 2 receptor. Comps. and methods for detecting and using these CSF2RB markers in a variety of clin. applications are disclosed. Such applications include methods for testing an individual for susceptibility for an adverse hematol. response, methods of selecting the appropriate drug therapy for patients based on the presence or absence of a CSF2RB marker, and products comprising a drug with hematol. toxicity that are approved for treating patients lacking a genetic marker.

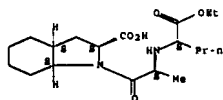
IT 107133-36-9, Perindopril erbumine
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); US88 (Uses)
 (genetic markers in CSF2RB gene associated with adverse hematol. response to drugs, and genotyping for drug risk assessment)

RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMP C19 H32 N2 OS

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
 CMP C4 H11 N



LE: ANSWER 52 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2006-795048 CAPLUS Full-text
 DN 145-230398

TI 1-Acylamino-2-hydroxy-3-amino-N-arylaalkanes as renin inhibitors and their preparation, pharmaceutical compositions and their use for treatment of hypertension

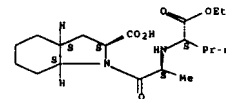
10576386

102 of 361

(hydroxylated nebivolol metabolites for increase of NO release from endothelium in combination with other agent(s) for treating and/or preventing vascular diseases)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LE ANSWER 51 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2006-796152 CAPLUS Full-text
 DN 145-230399

TI Genetic markers in the CSF2RB gene associated with an adverse hematological response to drugs
 IN Alachoulou, Maria; Gerson, Stanton
 PA USA
 SO U.S. Pat. Appl. Publ., 38pp.
 CODEN: USXXCO

DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006178843	A1	20060810	US 2006-351371	20060209
AU 2006213677	A1	20060817	AU 2006-213677	20060209
CA 2597259	A1	20060817	CA 2006-2597259	20060209
WO 2006086748	A2	20060817	WO 2006-US4960	20060209
WO 2006086748	A3	20061231		
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PA, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SN, SY, TJ, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1853909	A2	20071114	EP 2006-734885	20060209
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI US 2005-651834P	P	20050209		
US 2006-US4960	M	20060209		

10576386

104 of 361

IN Mcgeehan, Gerard; Simpson, Robert D.; Zeng, Menguang; Baldwin, John J.; Claremon, David A.; Dillard, Lawrence W.; Ianchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; Capatian, Slavation; Tice, Colin; Zhao, Wei
 PA Vitae Pharmaceuticals, Inc., USA
 SO PCT Int. Appl., 149pp.
 CODEN: PIXXD2

DT Patent
 LA English
 FAN.CNT 1

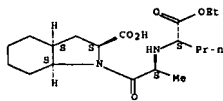
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006083924	A1	20060810	WO 2006-US3489	20060201
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PA, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SN, SY, TJ, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2596444	A1	20060810	CA 2006-2596444	20060201
EP 1844002	A1	20071017	EP 2006-720036	20060201
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI US 2005-649361P	P	20050202		
US 2006-US3489	M	20060201		
OS MARPAT 145-230398				
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 1-Acylamino-2-hydroxy-3-amino-N-arylaalkanes of formula I and the salts thereof, have renin-inhibiting properties and can be used as antihypertensive, medicinally active ingredients. Comps. of formula I wherein R1 is H, halo, halo, lower alkoxy, cycloalkoxy, etc.; R2 and R3 are independently H, halo, CN, carbamoyl, lower (halo)alkyl, etc.; R4 is H, lower alkyl, OH, lower alkoxy, cycloalkoxy, etc.; R5 and R6 or R3 and R4 taken together with the atoms they are attached form a fused (un)substituted dioxolane, (un)substituted dioxane, (un)substituted benzene or (un)substituted cyclohexene; R5 is lower (halo)alkyl, (halo)cycloalkyl, lower (halo)alkyl-cycloalkyl, aryl, heterocyclyl, etc.; R6 is amino, lower (dialkylamino, or lower alkanoylamino, R7 is H, lower (halo)alkylcycloalkyl, or lower (halo)alkoxy-lower alkyl; X is methylene or hydroxymethylene; Q is CO, CS, or SO2; R8 is lower (halo)alkyl, C8-15 (halo)alkyl, (halo)cycloalkyl, lower alkyl-cycloalkyl, etc.; and the enantiomers, diastereoisomers and pharmaceutically acceptable salts thereof are claimed. Example compound II=HCl was prepared by aminolysis of compound III to give the corresponding diamino alc., which underwent amidation with cyclohexanecarboxylic acid to give tert-Bu (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-(cyclohexanecarbonyl)amino-2-hydroxy-6-methylheptan-3-ylcarbamate, which underwent acid hydrolysis to give compound I=HCl. All the invention comds. were evaluated for their renin inhibitory activity (no data).

IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of acylamino(hydroxy)amino-o-arylalkanes as renin-inhibitors useful as antihypertensive)
 RN 82834-16-0 CAPLUS
 CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

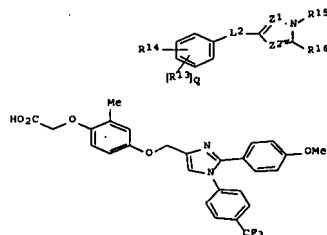


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 53 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM
 AN 2006795736 CAPLUS Full-text
 DN 145:230633
 TI Preparation of 4-[(benzimidazolyl)pyrazolyl(triazolyl)methoxy]phenoxyacetic acids as PPAR modulators
 IN Cow, Christopher; Eppler, Robert; Wang, Xing; Xie, Yongping
 PA Irm LL, Bermuda
 SO PCT Int. Appl., 62pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

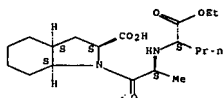
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006084176	A2	20060810	WO 2006-US3924	20060203
WO 2006084176	A3	20060914		
W:	AR, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SV, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BM, GH, GM, KE, LS, LM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
AU 2006210503	A1	20060810	AU 2006-210503	20060203
CA 2595789	A1	20060810	CA 2006-2595789	20060203
EP 1843763	A2	20071017	EP 2006-734339	20060203
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			

IN 2007DN05903 A 20070727 IN 2007-DN5903 20070727
 PRAI US 2006-045922 P 20060203
 WO 2006-US3924 W 20060203
 OS MARPAT 145:230633
 GI



AB The title compds. I (q = 0-3; Z1, Z2 = CH, N; L2 = XOX, XSOO-2X, XSOO-2XO (wherein X = a bond, (unsubstituted alkylene); R13 = halo, alkyl, alkoxy, etc.; R14 = XOX(O)OR17, XC(O)OR17 (X = a bond, alkylene; R17 = H, alkyl); R15, R16 = R18 or YR18 (Y = alkylene, alkenylene, alkynylene, CONR17, OX, X = a bond, alkylene; R17 = H, alkyl; R18 = cycloalkyl, heterocycloalkyl, aryl, heteroaryl); or R15 and R16 together with the atoms to which R15 and R16 are attached form fused bicyclic or tricyclic heteroaryl), useful in treating or preventing diseases or disorders associated with the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPAR δ (no specific data given), were prepared. Thus, reacting Me (4-hydroxy-2-methylphenoxy)acetate with 4-(chloromethyl)-2-(4-methoxyphenyl)-1-(4-trifluoromethylphenyl)-1H-imidazole (prepn. given) followed by hydrolysis afforded 28a II. Also disclosed are pharmaceutical compns. comprising compds. I alone or in combination with other therapeutic agents.
 IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of 4-[(benzimidazolyl)pyrazolyl(triazolyl)methoxy]phenoxyacetic acids as PPAR modulators for treating and preventing diseases-associated with PPAR activity, particularly activity of PPAR δ)
 RN 82834-16-0 CAPLUS
 CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

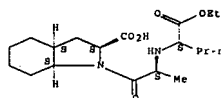
Absolute stereochemistry. Rotation (-).



LS ANSWER 54 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM
 AN 2006680403 CAPLUS Full-text
 DN 145:124844
 TI Process for the synthesis of (2S,3aS,7aS)-1-[(S)-alanyloctahydro-1H-indole-2-carboxylic acid derivatives and use in the synthesis of perindopril
 IN Kumar, Ashok; Soudagar, Satish Rajanikant; Mathur, Arpana; Gunjal, Sanjay Tukaram; Panda, Nalinakshya Balaram; Jadhav, Dilip Uttam
 PA IPCA Laboratories Limited, India
 SO Eur. Pat. Appl., 16 pp.
 CODEN: EPXDXM
 DT Patent
 LA English
 FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1679072	A1	20060712	EP 2005-113099	20051230
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU			
IN 2005MU00017	A	20050811	IN 2005-MU17	20050106
PRAI IN 2005-MU17	A	20050106		
OS CASREACT 145:124844				
AB The invention relates perindopril [(2S,3aS,7aS)-1-[(S)-1-(ethoxycarbonyl)butyl]amino]propionyl]octahydro-1H-indole-2-carboxylic acid] aralkyl ester salts used in the synthesis of perindopril. Thus, (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid was treated with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine in CH ₂ Cl ₂ in the presence of Et ₃ N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to afford 99% perindopril benzyl ester. Conversion of the latter into the oxalate salt, followed by hydrogenolysis over 5% Pd/C and reaction with tert-butylamine yielded perindopril erbumine. IT 107133-36-8P, Perindopril erbumine RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (process for synthesis of alanyloctahydroindolecarboxylic acid deriva. in synthesis of perindopril) RN 107133-36-8 CAPLUS CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME) CM 1 CRN 82834-16-0 CMP C19 H32 N2 O5				

Absolute stereochemistry. Rotation (-).

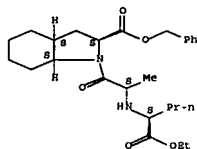


CM 2
 CRN 75-64-9
 CMP C4 H11 N



IT 122454-52-8P 897922-09-7P 897922-10-0P
 897922-11-1P 897922-12-2P 897922-13-3P
 897922-14-4P 897922-15-5P 897922-16-6P
 897922-18-8P 897922-19-9P 897922-20-2P
 897922-21-3P 897922-22-4P 897922-23-5P
 897922-24-6P 897922-25-7P 897922-26-6P
 897922-27-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (process for synthesis of alanyloctahydroindolecarboxylic acid deriva. in synthesis of perindopril)
 RN 122454-52-8 CAPLUS
 CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

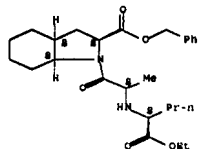


RN 897922-09-7 CAPLUS
 CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, ethanedioate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
 CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

CRN 144-62-7
 CMF C2 H2 O4

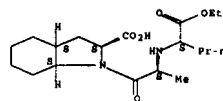


RN 897922-10-0 CAPLUS
 CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, ethanedioate (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 144-62-7
 CMF C2 H2 O4

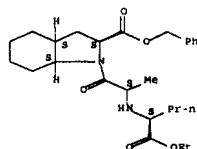


RN 897922-11-1 CAPLUS
 CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
 CMF C26 H38 N2 O5

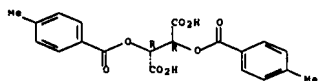
Absolute stereochemistry.



CM 2

CRN 32634-66-5
 CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).

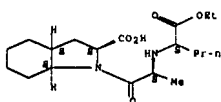


RN 897922-12-2 CAPLUS
 CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMF C19 H32 N2 O5

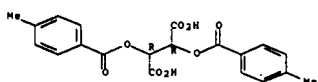
Absolute stereochemistry. Rotation (-).



CM 2

CRN 32634-66-5
 CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).



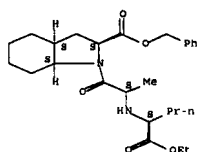
RN 897922-13-3 CAPLUS
 CN Butanedioic acid, 2,3-dihydroxy-, (2R,3R)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8

CMF C26 H38 N2 O5

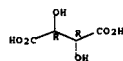
Absolute stereochemistry.



CM 2

CRN 87-69-4
 CMF C4 H6 O6

Absolute stereochemistry.

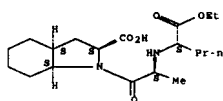


RN 897922-14-4 CAPLUS
 CN Butanedioic acid, 2,3-dihydroxy-, (2R,3R)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1

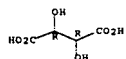
CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2
CRN 87-59-4
CMP C4 H6 O5

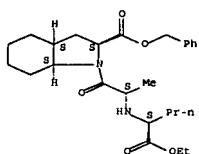
Absolute stereochemistry.



RN 897922-15-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, phosphate (1:?) (CA INDEX NAME)

CM 1
CRN 122454-52-8
CMP C26 H38 N2 O5

Absolute stereochemistry.



CM 2
CRN 7664-38-2
CMP H3 O4 P



RN 897922-16-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-,

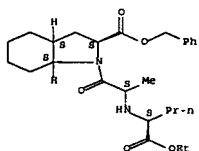
CM 2
CRN 88-99-3
CMP C8 H6 O4



RN 897922-19-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, (1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonate (1:?) (CA INDEX NAME)

CM 1
CRN 122454-52-8
CMP C26 H38 N2 O5

Absolute stereochemistry.



CM 2
CRN 3144-16-9
CMP C10 H16 O4 S

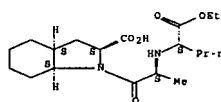
Absolute stereochemistry. Rotation (+).



phosphate (1:?) (CA INDEX NAME)

CM 1
CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



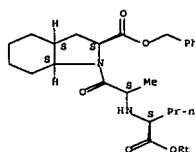
CM 2
CRN 7664-38-2
CMP H3 O4 P



RN 897922-18-8 CAPLUS
CN 1,2-Benzenedicarboxylic acid, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1
CRN 122454-52-8
CMP C26 H38 N2 O5

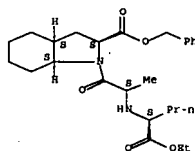
Absolute stereochemistry.



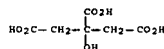
RN 897922-20-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:?) (CA INDEX NAME)

CM 1
CRN 122454-52-8
CMP C26 H38 N2 O5

Absolute stereochemistry.



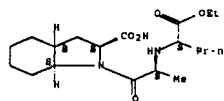
CM 2
CRN 77-92-9
CMP C6 H8 O7



RN 897922-21-3 CAPLUS
CN 1,2-Benzenedicarboxylic acid, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1
CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 88-99-3
CMP C8 H6 O4

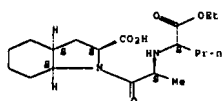
RN 897922-22-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, (1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonate (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

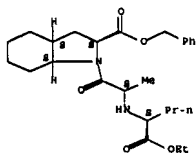
Absolute stereochemistry. Rotation (-).



CM 2

CRN 3144-16-9
CMP C10 H16 O4 S

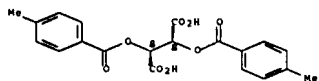
Absolute stereochemistry. Rotation (+).



CM 2

CRN 32634-68-7
CMP C20 H18 O8

Absolute stereochemistry. Rotation (+).



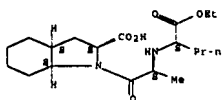
RN 897922-25-7 CAPLUS

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2



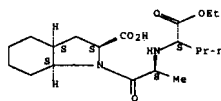
RN 897922-23-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:?) (CA INDEX NAME)

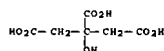
CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 77-92-9
CMP C6 H8 O7

RN 897922-24-6 CAPLUS

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

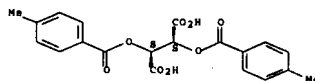
CM 1

CRN 122454-52-8
CMP C26 H38 N2 O5

Absolute stereochemistry.

CRN 32634-68-7
CMP C20 H18 O8

Absolute stereochemistry. Rotation (+).



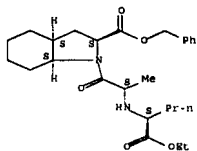
RN 897922-26-8 CAPLUS

CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2R,3R)-rel., compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMP C26 H38 N2 O5

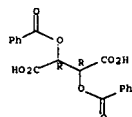
Absolute stereochemistry.



CM 2

CRN 22333-70-6
CMP C18 H14 O8

Relative stereochemistry.



RN 897922-27-9 CAPLUS

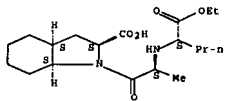
CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2R,3R)-rel-, compd. with (2S,3aS,7aS)-1-((2S)-2-(((1S)-1-(ethoxycarbonyl)butyl)amino)-1-oxopropyl)octahydro-1H-indole-2-carboxylic acid (1:7) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

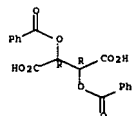


CM 2

CRN 22333-70-6

CMP C18 H14 O8

Relative stereochemistry.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L ANSWER 56 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:655550 CAPLUS Full-text

DN 145:83667

TI Process for preparing perindopril erbumine

IN Palomo Nicolau, Francisco; De Leon, Dorcas

PA Quimica Sintetica, S.A., Spain

SO PCT Int. Appl., 13 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006070276	A1	20060706	WO 2005-183928	20051119
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
ES 2255872	A1	20060701	ES 2004-3168	20041231
ES 2255872	B1	20070816		
EP 1833788	A1	20070919	EP 2005-818419	20051215
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			
PRAI ES 2004-3168	A	20041231		
WO 2005-183928	W	20051215		
OS CASREACT 145:83667				

AB A process for preparing perindopril erbumine, useful in the treatment of hypertension, comprises reacting an active ester of N-((1S)-((ethoxycarbonyl)butyl)-L-alanine with an organic salt of perhydroindole-2-carboxylic acid, followed by the addition of tert-butylamine. An example using the acetoxime as active ester in acetonitrile in the presence of phosphoric acid afforded 90% perindopril erbumine (99.5% purity).

IT 107133-36-9P, Perindopril erbumine

RU: IMP (Industrial manufacture); SPN (Synthetic preparation); PRSP (Preparation)

(preparation of perindopril erbumine)

RN 107133-36-8 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-((2S)-2-(((1S)-1-(ethoxycarbonyl)butyl)amino)-1-oxopropyl)octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

L ANSWER 55 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:677768 CAPLUS Full-text

DN 145:12211

TI Genotyping of PECAM-1 polymorphisms associated with risk of atherosclerosis and coronary heart disease

IN Chatterjee, Suboto; Heming, Wei

PA The Johns Hopkins University, USA

SO PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006074405	A2	20060713	WO 2006-05525	20060105
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRAI US 2005-641595P

AB The invention relates to methods of identifying inter-patient differences in genotype of PECAM-1 to diagnose and assess risk of arterial disease. Two single nucleotide polymorphisms in the PECAM-1 gene, Leu125Val (c373g) and Ser563Asn (g1688a), are associated with coronary heart disease in an Asian Indian population. Ren cells transfected with wild-type and/or 125-Val and 563-Asn gene polymorphisms exhibit increased PECAM-1 protein levels associated with variant haplotype. The invention further relates to methods of identifying therapeutic agents for to treat coronary arterial disease, and to methods for determining and exploiting such differences to improve medical outcomes.

IT 82634-16-0, Perindopril

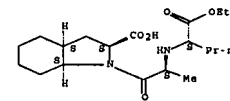
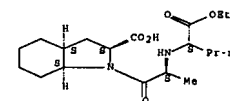
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(selection of and responsiveness to; genotyping of PECAM-1 polymorphisms associated with risk of atherosclerosis and coronary heart disease)

RN 82834-16-0 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-((2S)-2-(((1S)-1-(ethoxycarbonyl)butyl)amino)-1-oxopropyl)octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L ANSWER 57 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:634691 CAPLUS Full-text

DN 145:124588

TI Preparation of pyrazolopyrimidines as inhibitors of kinase activity

IN Coulter, Thomas Stephen; Taylor, Steven; Murfin, Stephen; Thammalakaa, Valery; Aicher, Babette; Jaekel, Stefan; Reuter, Tanja

PA Develogen Aktiengesellschaft, Germany; Evotec A.-G.

SO PCT Int. Appl., 122 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006066937	A2	20060629	WO 2005-EP13907	20051222
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
EP 1746099	A1	20070124	EP 2004-30674	20041223
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

IR, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU

EP 1927444 A2 20070905 EP 2005-022979 20051222

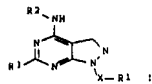
R1: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRAI EP 2004-30674 A 20041223

WO 2005-EP1907 W 20051222

GB MARPAT 146:124588

GI



AB The present invention relates to the use of pyrazolopyrimidine compds. (I; R1 = substituted C6-10 aryl or optionally substituted C5-10 heteroaryl, wherein the substituents are one or more of R4; R4 = halogen, cyano, CO2R5, OR5, C(O)N(R5R5a), S(O)2N(R5R5a), S(O)N(R5R5a), S(O)2R5, N(R5)S(O)2N(R5R5a), SR5, N(R5R5a), OC(O)R5, N(R5)C(O)R5a, N(R5)S(O)2R5a, etc.; R5, R5a = H, C1-10 cycloalkyl, C4-10 bicycloalkyl, C4-10 heterocyclyl, (un)substituted C1-6 alkyl, etc.; R2 = H, C1-4 alkyl, acetyl, urea; R3 = H, hydroxy, C1-4 alkyl, amino; X = a bond) or metabolites, prodrugs or pharmaceutically acceptable salts thereof, and optionally a pharmaceutically acceptable carrier for the preparation of pharmaceutical compns. for inhibiting the activity of the kinase activity of Mnk1 or Mnk2 (Mnk2a, Mnk2b) or variants thereof or for the prophylaxis and/or treatment of diseases which can be influenced by the inhibition of the kinase activity of Mnk1 and/or Mnk2 (Mnk2a or Mnk2b) and/or variants thereof. The above diseases include diseases of the carbohydrate and/or lipid metabolism and their consecutive complications and diseases, e.g. impaired glucose tolerance, diabetes mellitus type II, latent autoimmune diabetes in adults (LADA), diabetes mellitus type I, obesity, metabolic syndrome, eating disorders, cachexia, osteoarthritis, biliary stones, and diabetic complications (carbohydrate metabolic diseases) and hypercholesterolemia, dyslipidemia familial hypercholesterolemia, Fredrickson's hyperlipoproteinemia, and cardiovascular diseases (lipid metabolic diseases). Thus, [4-(pyrrol-1-yl)phenyl]hydrazine hydrochloride was treated with MeOEt in ethanol at room temperature and cyclized with (ethoxycarbonyl)malononitrile under refluxing for 2 h to give 88 5-amino-1-[4-(pyrrol-1-yl)phenyl]-1H-pyrazole-4-carbonitrile which was cyclized with formamide at 180° for 3 h to give 114 [1-[4-(pyrrol-1-yl)phenyl]-1H-pyrazolo[3,4-d]pyrimidin-4-yl]amine (II).

IT 82834-16-0, Perindopril

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; preparation of pyrazolopyrimidines as inhibitors of Mnk1 or Mnk2 (Mnk2a or Mnk2b) kinase activity)

RN 82834-16-0 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

CM 2

CRN 75-64-9

CMF C4 H11 N



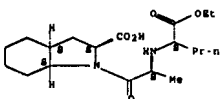
IT 82834-16-0, Perindopril

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of perindopril erbumine crystal type I)

RN 82834-16-0 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



ANSWER 59 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:597465 CAPLUS Full-text

DN 146:100554

TI New procedure for preparation of perindopril in new crystal form

IN Rucman, Rudolf

PA Diagen D.O.O. Slovenia

SO Slov., 16pp.

CODEN: SIXXAW

DT Patent

LA Slovenian

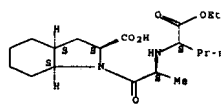
PAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
SI 21801	A	20051231	SI 2004-181	20040621
PRAI SI 2004-181		20040621		

GB CASREACT 146:100554; MARPAT 146:100554

AB The submitted invention deals with a synthesis of the ACE inhibitor perindopril, starting from a stereospecific amino acid N-[(S)-carboxy-1-butyl]-[(S)-alanine, which is protected with a trimethylsilyl group and then transformed into a reactive acidic bromide or fluoride which in the final

Absolute stereochemistry. Rotation (-).



ANSWER 58 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:627685 CAPLUS Full-text

DN 145:89824

TI Preparation of perindopril erbumine crystal type I

IN Kiuchi, Yasuyuki; Yokogoshi, Kiyonori

PA Pharmachem Asia, Ltd., Japan

SO Jpn. Kokai Tokkyu Koho, 15 pp.

CODEN: JKXXAP

DT Patent

LA Japanese

PAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006169169	A	20060629	JP 2004-364224	20041216
PRAI JP 2004-364224		20041216		

AB This invention relates to industrial manufacturing method for novel crystal type perindopril erbumine (I) with high purity and high yield. The I is treated with THF or perindopril is reacted with tert-butylamine in THF solvent to form crystalline I type I.

IT 107133-36-8P, Perindopril erbumine

RL: IMF (Industrial manufacture); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of perindopril erbumine crystal type I)

RN 107133-36-8 CAPLUS

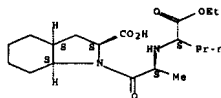
CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



phase reacts with (2S,3aS,7aS)-octahydroindol-2-carboxylic acid with the trimethylsilyl protection on the carboxylic group to obtain perindopril after removal of protection groups.

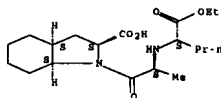
IT 82834-16-0P, Perindopril

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of perindopril in new crystal form)

RN 82834-16-0 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



ANSWER 60 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:469692 CAPLUS Full-text

DN 144:460880

TI Nitrosated and nitrosylated compounds, compositions, and methods for the treatment of ophthalmic disorders

IN Letts, L. Gordon; Garvey, David S.

PA Nitromed, Inc., USA

SO PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DT Patent

LA English

PAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006052899	A2	20060518	WO 2005-US40314	20051108
WO 2006052899	A3	20061116		

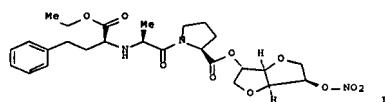
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, ME, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GM, GN, GW, HT, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, GM, KE, LS, LM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

NO.	DATE	NO.	DATE
AU 2005304770	A1	20060518	AU 2005-304770
CA 2576279	A1	20060518	CA 2005-2576279
EP 1814535	A2	20070808	EP 2005-826100

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

10576386 129 of 361
 PRAI US 2004-625578P P 20041108
 WO 2005-054031.4 W 20051108
 OS MARPAT 144:460880
 GI



AB The invention describes nitrosated and/or nitrosylated compds. or pharmaceutically acceptable salts thereof, and compns. comprising at least one nitrosated and/or nitrosylated compound, and, optionally, at least one nitric oxide donor and/or at least one therapeutic agent. The invention also provides compns. and kits comprising at least one compound of the invention, that is optionally nitrosated and/or nitrosylated, and, optionally, at least one nitric oxide donor compound and/or at least one therapeutic agent. The invention also provides methods for treating ophthalmic disorders. The nitrosated and/or nitrosylated compds. are preferably nitrosated and/or nitrosylated adrenergic antagonists and nitrosated and/or nitrosylated angiotensin-converting enzyme (ACE) inhibitors. Preparation of I is described.

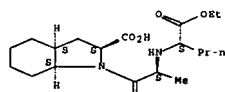
IT 82834-16-05, Perindopril, nitrosated and nitrosylated derivs.
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nitrosated and nitrosylated compds. for treatment of ophthalmic disorders)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



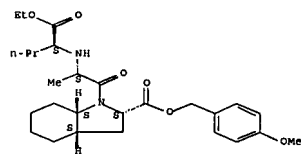
ANSWER 61 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2006:386591 CAPLUS Full-text
 DN 144:412896

10576386 131 of 361

RN 793716-57-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (4-methoxyphenyl)methyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ANSWER 62 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2006:356970 CAPLUS Full-text
 DN 144:398255

TI Preparation of hydrated crystalline forms of perindopril erbumine and pharmaceutical formulations

IN Rucman, Rudolf; Zupet, Pavel

PA Diagen Smartno Prikljani, d.o.o., Slovenia

SO Eur. Pat. Appl., 17 pp.

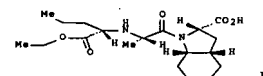
CODEN: EPKXDM

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1647547	A1	20060419	EP 2005-468015	20051013
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU			
SI 21881	A	20060410	SI 2004-285	20041015
PRAI SI 2004-285	A	20041015		



10576386 130 of 361

TI Preparation of perindopril precursor and perindopril erbumine
 IN Kiuchi, Yasuyuki; Yokogoshi, Kiyonori
 PA Pharmacia Asia Ltd., Japan
 SO Jpn. Kokai Tokkyo Koho, 17 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2006111579	A	20060427	JP 2004-301012	20041015
PRAI JP 2004-301012		20041015		

OS MARPAT 144:412896

AB Perindopril p-methoxybenzyl ester (I) is prepared from (2S,3aS,7aS)-2-carboxyoctahydroindole (II) via BOC-II and its p-methoxybenzyl ester. Acid hydrolysis of I and treatment with Me3CNH2 give perindopril erbumine. Thus, protection of II with di-tert-Bu dicarbonate gave 91% BOC-II, which was esterified with p-ClCH2C6H4OMe to afford 92% p-methoxybenzyl ester. The ester was deprotected by methanesulfonic acid and amidated with (S)-EtO2CCHPr-L-Ala to give I.

IT 107133-36-0F, Perindopril erbumine 793716-57-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(Preparation of perindopril erbumine via p-methoxybenzyl ester)

RN 107133-36-0 CAPLUS

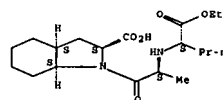
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



10576386 132 of 361

AB The object of the invention are new crystalline forms perindopril erbumine (I.Me3CNH2) monohydrate, I.Me3CNH2 sesquihydrate and I.Me3CNH2 dihydrate and a process for the preparation thereof by dissolving I.Me3CNH2 in water or in water with the addition of a volatile water-miscible polar organic solvent, freezing and lyophilizing. Another object of the invention is a new process for the preparation of perindopril erbumine monohydrate in pure crystalline form by freezing aqueous acetone solns. and lyophilizing. Another object of the invention are pharmaceutical formulations for the treatment of arterial hypertension and with vasodilatory activity, containing a therapeutically effective amount of these new crystalline forms.

IT 107133-36-0, Perindopril erbumine 690267-97-1

882674-51-3 882674-53-5, Perindopril erbumine

sesquihydrate

RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(preparation of hydrated crystalline forms of perindopril erbumine and pharmaceutical formulations)

RN 107133-36-0 CAPLUS

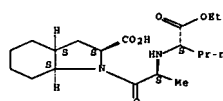
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



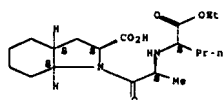
RN 690267-97-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd.

10576386 133 of 361
with 2-methyl-2-propanamine, hydrate (1:1:1) (CA INDEX NAME)

CM 1
CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



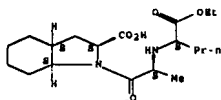
CM 2
CRN 75-64-9
CMP C4 H11 N



RN 882674-51-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1:1), dihydrate (9CI) (CA INDEX NAME)

CM 1
CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



10576386 134 of 361

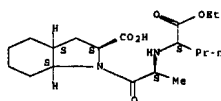
CM 2
CRN 75-64-9
CMP C4 H11 N



RN 882674-53-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine, hydrate (2:2:3) (9CI) (CA INDEX NAME)

CM 1
CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2
CRN 75-64-9
CMP C4 H11 N



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 63 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM
2006:342911 CAPLUS [Full-text](#)
DN 144:382027
TI Angiotensin receptor signal transduction inhibitors for treating

10576386 135 of 361

otospogoniosis
IN Imauchi, T. et al.
PA Japan
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006038265	A1	20060413	WO 2004-JP14390	20040930
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SV, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

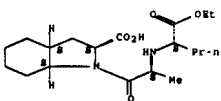
AB It is intended to provide a medicinal composition for treating otospogoniosis, a method of determining its dose, a method of administering the same and a diagnostic marker for otospogoniosis. As a diagnostic marker for otospogoniosis, DNA is isolated from a human subject and the genotype of the allele at the M235T polymorphism in angiotensinogen gene is examined by PCR. Based on the results thus obtained, the cause of otospogoniosis is estimated in the case where otospogoniosis is seemingly caused by the hyperactivity of an angiotensinogen receptor, a drug compound capable of lowering the activity is administered to the patient.

IT 107133-36-2, Perindopril erbumine
RI: PAC (Pharmacological activity), THU (Therapeutic use), BIOL (Biological study), USRS (Uses)
(angiotensin II receptor signal transduction inhibitors for treatment of otospogoniosis)

RN 107133-36-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1:1) (CA INDEX NAME)

CM 1
CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



10576386 136 of 361

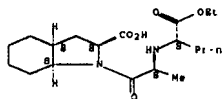
CM 2
CRN 75-64-9
CMP C4 H11 N



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 64 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM
2006:269508 CAPLUS [Full-text](#)
DN 144:331420
TI Preparation of bicyclic anilide spirolactam cgrp receptor antagonists
IN Bell, Ian M.; Theberge, Cory R.; Stump, Craig A.; Zhang, Xufang; Gallicchio, Steven N.; Zartman, C. Blair
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006031610	A2	20060323	WO 2005-US32041	20050909
WO 2006031610	A3	20060831		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SV, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GM, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005285109	A1	20060323	AU 2005-285109	20050909
CA 2579847	A1	20060323	CA 2005-2579847	20050909
EP 1797073	A2	20070620	EP 2005-795448	20050909
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101018781	A	20070813	CN 2005-80030605	20050909
IN 2007DN01493	A	20070813	IN 2007-DN1493	20070223
PRAI US 2004-609292P	P	20040613		
WO 2005-US32041	W	20050909		
OS MARPAT 144:331420				
GI				



CM 2

CRN 75-64-9
CMP C4 H11 NRE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT✓
ANWHER 67 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
2005:1311320 CAPLUS Full-textDN 144:7101
TI Method for synthesis of perindopril and its pharmaceutically acceptable salts

IN Fugier, Claude; Dubuffet, Thierry; Langlois, Pascal

PA Adir et Compagnie, Fr.; Les Laboratoires Servier

SO Eur. Pat. Appl., 9 pp.

CODEN: EPXXDM

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1367063	A1	20031203	EP 2003-291931	20030731
EP 1367063	B1	20060823		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 337332	T	20060915	AT 2003-291931	20030731
ES 2271498	T3	20070416	ES 2003-3291931	20030731
AU 2004261439	A1	20050210	AU 2004-261439	20040729
CA 2533005	A1	20050210	CA 2004-2533005	20040729
WO 2005012333	A2	20050210	WO 2004-FR2035	20040729
WO 2005012333	A3	20050324		
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

RW: BM, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CN 1826352	A	20060830	CN 2004-80021209	20040729
BR 2004013169	A	20061003	BR 2004-13169	20040729
JP 2007526896	T	20070920	JP 2006-521621	20040729
IN 2006DN00460	A	20070831	IN 2006-DN460	20060127
MX 2006PA01243	A	20060411	MX 2006-PA1243	20060131
US 2006183920	A1	20060817	US 2006-566562	20060131
NO 2006000922	A	20060224	NO 2006-922	20060224
PRAI EP 2003-291931	A	20030731		
WO 2004-FR2035	W	20040729		
OS MARPAT 144-7101				

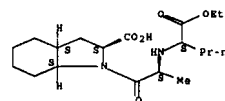
AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed by catalytic hydrogenation. In an example, the resp. coupling reactions were carried in CH₂Cl₂-Et₃NPr-i2 at room temperature and MeCN-Et₃N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).

IT 22834-16-UP 107133-36-AP
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

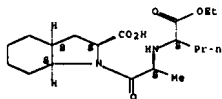
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

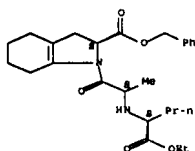
CRN 75-64-9
CMP C4 H11 N

IT 22834-16-UP 107133-36-AP
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)

RN 539820-43-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

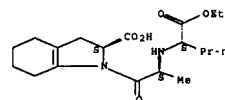
Absolute stereochemistry.



RN 625095-50-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT✓
ANWHER 68 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
2005:1311047 CAPLUS Full-text

DN 144:7100

TI Method for synthesis of perindopril and its pharmaceutically acceptable salts

IN Fugier, Claude; Dubuffet, Thierry; Langlois, Pascal

PA Adir et Compagnie, Fr.; Les Laboratoires Servier

SO Eur. Pat. Appl., 9 pp.

CODEN: EPXXDM

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1367062	A1	20031203	EP 2003-291930	20030731
EP 1367062	B1	20060830		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 338058	T	20060915	AT 2003-291930	20030731
ES 2271497	T3	20070416	ES 2003-3291930	20030731
AU 2004261440	A1	20050210	AU 2004-261440	20040729
WO 2005012328	A2	20050210	WO 2004-FR2036	20040729
WO 2005012328	A3	20050324		
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BM, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

CN 1826351	A	20060830	CN 2004-80021208	20040729
JP 2006528653	T	20061221	JP 2006-521622	20040729
IN 2006DN00468	A	20070831	IN 2006-DN468	20060127
US 2006189813	A1	20060824	US 2006-566558	20060131
PRAI EP 2003-291930	A	20030731		
WO 2004-FR2036	W	20040729		

OS CASREACT 144-7100; MARPAT 144-7100

AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl

ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed by catalytic hydrogenation. In an example, the resp. coupling reactions were carried in CH₂Cl₂-Et₃N at room temperature and MeCN-Et₃N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine

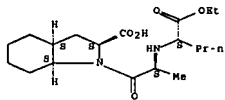
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



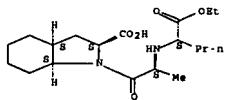
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMP C4 H11 N

TI Thiazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy

IN Epple, Robert; Cow, Christopher; Xie, Yongping; Wang, Xing; Russo, Ross; Azinovic, Mihai; Saez, Enrique

PA IRM LLC, Bermuda

SO PCT Int. Appl., 187 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005116000	A1	20051208	WO 2005-US18167	20050524
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005247931	A1	20051208	AU 2005-247931	20050524
CA 2563818	A1	20051208	CA 2005-2563818	20050524
EP 1748993	A1	20070207	EP 2005-754130	20050524
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1980906	A	20070613	CN 2005-80016538	20050524
US 2007203155	A1	20070830	US 2006-597282	20061121
KR 2007030791	A	20070316	KR 2006-724606	20061123
IN 2006CN04307	A	20070615	IN 2006-CN4307	20061123
NO 2006005984	A	20070705	NO 2006-5984	20061222
PRAI US 2004-574137P	P	20040724		
US 2005-648985P	P	20050131		
WO 2005-US18167	W	20050524		
OS MARPAT 144:36329				
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to thiazole compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPAR δ . In compds. I, p is 0-3; L is selected from -XOX-, -XS(O)MX-, and -XS(O)MXO-, where m is 0-2 and X is a bond or (un)substituted C1-4 alkylene; R1 is selected from halo, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl, C1-6 haloalkyl, C1-6 haloalkoxy, (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl, (un)substituted C3-12 cycloalkyl, and (un)substituted C3-8 heterocyclyl, R2 is -XOCOR5 or -XOCOR5, where X is as defined previously and R5 is H or C1-6 alkyl; and R3 and R4 are independently selected from R6 and R6Y, where R6 is (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13 heteroaryl, and Y is selected from C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene, -C(O)N(R5)-, and -OX-, where X and R5 are as defined previously, or R3 and R4, together with the atoms to which they are attached, form fused



IT 539820-43-4P 625095-50-3P

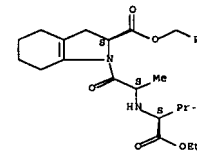
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)

RN 539820-43-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

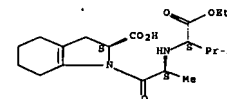
Absolute stereochemistry.



RN 625095-50-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 69 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
2005:1290025 CAPLUS Full-text
DN 144:36329

bi- or tricyclic C5-14 heteroaryl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Cyclocondensation of 2-bromo-4'-methoxyacetophenone with thioacetamide followed by bromination, demethylation, and alkylation with iso-Pr iodide gave bromothiazole II, which was brominated and substituted with phenol III (preparation in 3 steps from 4-hydroxy-3-methylacetophenone given) to give thiazole IV. Compound IV underwent Suzuki coupling with 4-(trifluoromethoxy)phenylboronic acid and ester hydrolysis to give thiazole V. Most preferred compds. of the invention express an EC50 value for PPAR δ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPAR δ over PPAR γ .

IT 82834-16-0, Perindopril

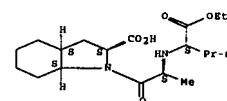
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of thiazole compds. as PPAR modulators and their use for treatment and prevention of diseases associated with PPAR δ activity)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 70 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
2005:1289979 CAPLUS Full-text
DN 144:36326

TI Thiazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy

IN Epple, Robert; Xie, Yongping; Wang, Xing; Cow, Christopher; Russo, Ross

PA IRM LLC, Bermuda

SO PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005116016	A1	20051208	WO 2005-US18166	20050524
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,				

LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RM: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2005247930 A1 20051208 AU 2005-247930 20050524
 CA 2563819 A1 20051208 CA 2005-2563819 20050524
 EP 1749003 A1 20070207 EP 2005-775612 20050524

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, ML, PL, PT, RO, SE, SI, SK, TR

CN 1980919 A 20070611 CN 2005-8016511 20050524
 KR 2007043705 A 20070425 KR 2006-724605 20061123
 IN 2006CM04108 A 20070615 IN 2006-CM4308 20061123
 NO 2006050983 A 20071005 NO 2006-5983 20061222
 US 2007244130 A1 20071018 US 2007-597260 20070705

PRAI US 2004-574137P P 20050524
 US 2005-649671P P 20050524
 WO 2005-081816 W 20050524

OR MARPAT 144:36326
 OI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to oxazole compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPAR δ . In compds. I, p is 0-3; L is selected from -XOX-, -XS(O)M-, and -XS(O)MXO-, where m is 0-2 and X is a bond or (un)substituted C1-4 alkylene; R1 is selected from halo, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl, C1-6 haloalkyl, C1-6 haloalkoxy, (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl, (un)substituted C3-12 cycloalkyl, and (un)substituted C3-8 heterocyclyl; R2 is -XOXCO2R5 or -XCO2R5, where X is as defined previously and R5 is H or C1-6 alkyl; and R3 and R4 are independently selected from R6 and R6Y, where R6 is (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13 heteroaryl, and Y is selected from C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene, -C(O)N(R5)-, and -OX-, where X and R5 are as defined previously, or R3 and R4, together with the atoms to which they are attached, form fused bi- or tricyclic C5-14 heteroaryl, including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Disoatization of 4-(trifluoromethoxy)acetophenone followed by heterocyclization with acetonitrile, and bromination gave bromooxazole II, which was brominated and substituted with phenol III (preparation in 3 steps from 4-hydroxy-3-methylacetophenone given) to give oxazole IV. Compound IV underwent Suzuki coupling with 2-isopropoxyphenylboronic acid (preparation from 2-chloro-5-bromopyridine given) and ester hydrolysis to give oxazole V. Most preferred compds. of the invention express an EC50 value for PPAR δ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPAR δ over PPAR γ .

HR, LV, MK, YU

NO 2006005695 A 20061211 NO 2006-5695 20061211

PRAI SI 2004-143 A 20040514
 SI 2004-235 A 20040805
 WO 2005-EP5048 W 20050510

OR CABREACT 144:7098; MARPAT 144:7098

AB The invention relates to a process for the preparation of the ACE inhibitor perindopril, its pharmaceutically-acceptable salts and intermediates obtained in the process. The process involves conversion of N-[(1S)-1-carbethoxybutyl]-L-alanine to the acid chloride hydrochloride and reaction with (2S,3aS,7aS)-octahydroindole-2-carboxylic acid or an ester or salt. The examples describe the synthesis of perindopril erbumine by reactions carried out in CH2Cl2.

IT 02034-16-OP, Perindopril 107133-36-9P, Perindopril erbumine 120465-02-3P 122454-52-8P
 069877-96-3P 069954-04-1P 069954-08-5P
 069954-09-6P

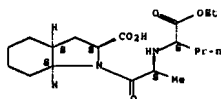
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for preparation of perindopril and its salts)

RN 02034-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

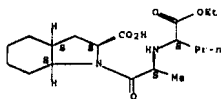
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 02034-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



IT 02034-16-0, Perindopril

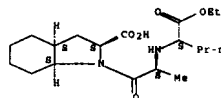
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of oxazoles as PPAR modulators and their use for treatment and prevention of diseases associated with PPAR δ activity)

RN 02034-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS NUMBER 71 OF 106 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:1262577 CAPLUS Full-text

DN 144:7098

TI Process for the preparation of perindopril and its salts

IN Mersalovic, Marjot; Svid, Janja; Tomsic, Zdenka

PA Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia

SO PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005113500	A1	20051201	WO 2005-EP5048	20050510
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
SI 21800	A	20051231	SI 2004-143	20040514
SI 21852	A	20060228	SI 2004-235	20040805
AU 2005245087	A1	20051201	AU 2005-245087	20050510
CA 2566754	A1	20051201	CA 2005-2566754	20050510
EP 1753720	A1	20070221	EP 2005-748048	20050510
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA,			

CM 2

CRN 75-64-9

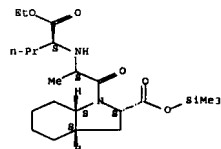
CMF C4 H11 N



RN 120465-02-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, trimethylsilyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

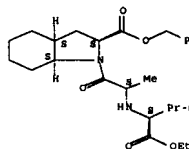
Absolute stereochemistry.



RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

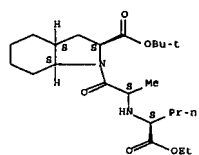
Absolute stereochemistry.



RN 869877-96-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

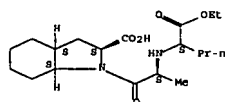
Absolute stereochemistry.



RN 869954-04-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monopotassium salt, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 869954-08-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monolithium salt, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

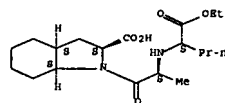
ZA, ZM, ZW
 RM: BW, GH, GM, KE, LS, MN, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2005245418 A1 20051201 AU 2005-245418 20050513
 CA 2564365 A1 20051201 CA 2005-2564365 20050513
 EP 1756062 A1 20070228 EP 2005-751010 20050513
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
 CN 1980894 A 20070613 CN 2005-80019645 20050513
 BR 2005010024 A 20070615 BR 2005-10024 20050513
 IN 2006CN04198 A 20070615 IN 2006-CN4198 20061114
 US 2007259890 A1 20070615 US 2006-596598 20061114
 PRAI US 2004-571004P P 20040514
 WO 2005-US16747 W 20050513
 OS MARPAT 144:22712
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to aryl compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPAR δ . In compds. I, m is 0-3; X, Y, and Z are independently selected from CH and N; L is (un)substituted (CH₂)_n(CH₂)_n or (CH₂)_n(O)(CH₂)_n, where each n is independently selected from 0-4 and p is 0-2; R₁ and R₂ are independently selected from (un)substituted C₃-12 cycloalkyl-A-, (un)substituted C₃-8 heterocyclyl-A-, (un)substituted C₆-10 aryl-A-, and (un)substituted C₃-8 heterocyclyl, and R₄ is selected from (CH₂)_n(CH₂)_nCO₂R₅ and (CH₂)_nCO₂R₅, where n is as defined previously and R₅ is H or C₁-6 alkyl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Substitution of Me bromoacetate with 4-hydroxy-3-methylacetophenone followed by Baeyer-Villiger oxidation and methanolysis gave phenoxylacetate II, which underwent substitution of 2,5-dibromobenzyl bromide to give dibromobenzyl ether III. Treatment of III with an excess of 4-trifluoromethylphenylboronic acid and ester hydrolysis resulted in the formation of terphenyl IV. Most preferred compds. of the invention express an EC₅₀ value for PPAR δ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPAR δ over PPAR α .

IT 82824-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOD (Biological study); USES (Uses)
 (preparation of triaryl compds. as PPAR modulators and their use for treatment and prevention of diseases associated with PPAR δ activity)

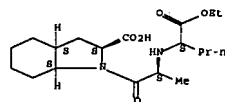
RN 82824-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA



RN 869954-09-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, sodium salt (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



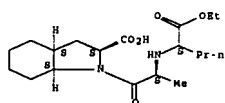
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 72 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2005:1262399 CAPLUS Full-text
 DN 144:22712
 TI Triaryl compounds as PPAR modulators, their preparation, pharmaceutical composition, and use in therapy
 IN Eppie, Robert; Azimioara, Mihai
 PA Irm LLC, Bermuda
 SO PCT Int. Appl., 59 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005113506	A1	20051201	WO 2005-US16747	20050513
N:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,			

INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 73 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2005:1259663 CAPLUS Full-text
 DN 144:22911
 TI Isoxazole compounds as PPAR modulators, their preparation, pharmaceutical composition, and use in therapy
 IN Eppie, Robert; Russo, Ross; Azimioara, Mihai; Xie, Yongping
 PA Irm LLC, Bermuda
 SO PCT Int. Appl., 79 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

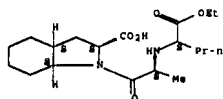
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005113519	A1	20051201	WO 2005-US16672	20050512
N:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	BW, GH, GM, KE, LS, MN, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2005245411	A1	20051201	AU 2005-245411	20050512
CA 2564429	A1	20051201	CA 2005-2564429	20050512
EP 1745027	A1	20070124	EP 2005-769154	20050512
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR			
CN 1984894	A	20070620	CN 2005-80019652	20050512
KR 2007034993	A	20070629	KR 2006-723769	20061113
IN 2006CN04201	A	20070622	IN 2006-CN4201	20061114
PRAI US 2004-571003P	P	20040514		
WO 2005-US16672	W	20050512		
OS MARPAT 144:22911				
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to isoxazole compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPAR δ . In compds. I, R1 is selected from (un)substituted C1-6 alkyl, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; R2 is selected from (CH₂)_n(CH₂)_nOR₃, (CH₂)_nOR₃, CO₂R₃, C(O)N(R₄)₂, C(O)N(R₄)(CH₂)_nOR₄, CO₂(CH₂)_nOR₃, C(O)N(R₄)(CH₂)_nOR₃, C(O)N(R₄)(R₅), and C(O)N(R₄)(CH₂)_nR₅, where n is 0-4, R₄ is H or C1-6 alkyl, and R₅ is C1-6 alkyl, C3-12 cycloalkyl, C3-8 heterocyclyl, C6-10 aryl, or C5-10 heteroaryl, or R₄ and R₅, together with the nitrogen atom to which they are attached, form C3-8 heterocyclyl or C5-10 heteroaryl; and R₃ is selected from (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl, including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Esterification of 3-bromophenylacetic acid followed by coupling with cyanide, reduction of the nitrile to an aldehyde, condensation with hydroxylamine, and chlorination gave chloroxime II. N-Boc-2-bromoethylamine was substituted with 2,4-dichlorophenol followed by deprotection, amidation with Et benzoylacetate to give benzoylacetamide III, which underwent cyclocondensation with chloroxime II and ester hydrolysis, resulting in the formation of isoxazole IV. Most preferred compds. of the invention express an EC₅₀ value for PPAR δ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPAR δ over PPAR γ .

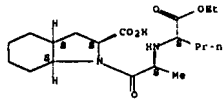
IT 62834-16-0 Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (compds. and compns. as PPAR modulators and their use for treatment and prevention of diseases associated with activity of PPAR families, particularly PPAR δ)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 74 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM



CM 2

CRN 75-64-9
 CMP C4 H11 N



LS ANSWER 75 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM
 AN 2005-1177978 CAPLUS Full-text
 DN 143:446753

TI Pharmaceutical aerosol composition containing poorly water-soluble active agent, a non-ionic surfactant, and a phospholipid
 IN Jauernig, Jürgen; Lintz, Frank-Christophe; Keller, Manfred; Friedrich, Ingo
 PA Pari G.m.b.H., Germany
 SO U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of Appl. No. PCT/EP04/011571.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005244339	A1	20051103	US 2005-106999	20050419
DE 10347994	A1	20050616	DE 2003-10347994	20031075
WO 2005037246	A2	20050428	WO 2004-EP11571	20040414
WO 2005037246	A3	20051208		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: BW, GH, GM, KE, LB, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI DE 2003-10347994	A	20031015		
WO 2004-EP11571	A2	20040414		

AN 2005-1201076 CAPLUS Full-text
 DN 143:446810
 TI Processes for the preparation of alpha polymorph of perindopril erbumine
 IN Joshi, Narendra; Shriram, Bhurud; Shekhar Bhaskar; Rao, Kodali Eswara
 PA Glenmark Pharmaceuticals Limited, India
 SO U.S. Pat. Appl. Publ., 8 pp.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005250706	A1	20051110	US 2005-122731	20050505
WO 2005108365	A1	20051117	WO 2005-181233	20050506
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CO, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI IN 2004-MU531 A 20040607
 US 2004-572402P P 20040519
 OS MARPAT 143:446810

AB A process for the preparation of an alpha polymorph of perindopril erbumine is provided comprising (a) forming a solution comprising perindopril erbumine in one or more ketones; (b) heating the solution to reflux; and (c) cooling the solution to a temperature sufficient to form the alpha polymorph of perindopril erbumine. The alpha polymorphs of perindopril erbumine obtained herein have a high purity level.

IT 107133-36-8P, Perindopril erbumine
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (of perindopril erbumine α -polymorph)

RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CNF C19 H32 N2 O5

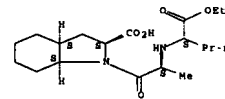
Absolute stereochemistry. Rotation (-).

AB Sterile compns. for administration as aerosols are described. They contain an active agent which is poorly water-soluble, a non-ionic surfactant a component and a phospholipid component. The compns. are suitable for oral or nasal inhalation, but also for topical or or mucosal administration. They are particularly useful for the efficient pulmonary administration of poorly soluble corticosteroids and can be aerosolized with common nebulizers. A colloidal solution contained cyclosporin 0.06, Tyloxapol 1.0, dimyristoyl phosphatidyl choline 1.0, propylene glycol 1.0, sodium chloride 0.7, and water for injection q.s. 100 mL. The average particle size of this colloidal solution was 9.7 nm.

IT 82834-16-0, Perindopril
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical aerosol composition)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LS ANSWER 76 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM
 AN 2005-1146100 CAPLUS Full-text
 DN 143:420385

TI Development of efficient genotyping method for detecting insertion/deletion type polymorphisms of human angiotensin converting enzyme gene
 IN Katsushita, Tomohiro; Sugimoto, Ken; Akasaka, Tadashi; Ogiwara, Toshio
 PA EBS K. K., Japan
 SO Jpn. Kokai Tokkyo Koho, 11 pp.
 CODEN: JXKXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2005295938	A	20051027	JP 2004-119417	20040414
PRAI JP 2004-119417		20040414		

AB An efficient genotyping method for detecting insertion/deletion type polymorphisms of human angiotensin converting enzyme gene. The method is designed to detect the polymorphisms in the extracted genomic DNA samples by the real time PCR using the specifically designed primers and probes with fluorometric (FRET) detection. The ACE gene polymorphism anal. is especially established for diagnostic prediction of the genetic susceptibility to cardiac infarction, cardiac hypertrophy, diabetic nephropathy, IGA nephropathy or purpura nephritis. The ACE genotypes are classified into the DD, ID and II types and the order of the susceptibility to the above mentioned diseases is DD > ID > II. The genotyping method is also applied to predict the

effectiveness of the ACE inhibitors in the therapy of hypertension. The order of the effectiveness of the ACE inhibitors is DD > ID > II. The ACE inhibitors that can be subjected to this effectiveness prediction are alacepril, imidapril hydrochloride, quinapril hydrochloride, temocapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, captopril,trandolapril, perindopril erbumine, enalapril maleate, lisinopril, lactotripeptide and the peptides from dried bonito or sardine.

IT

107133-36-8, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effectiveness dependent on genotype; development of efficient genotyping method for detecting insertion/deletion type polymorphisms of human angiotensin converting enzyme gene)

RN

107133-36-8 CAPLUS

CN

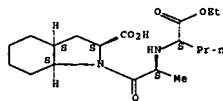
1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N



L8 ANSWER 77 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2005:1123812 CAPLUS Full-text

DN 143:379815

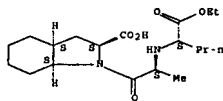
TI Method of reducing C-reactive protein using growth hormone secretagogues

IN Polvino, William J.; Carpi, David B.; Smith, Roy G.

PA Rejuvenon Corporation, USA

SO PCT Int. Appl. 135 pp.

CODEN: PIRXDD

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 78 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2005:1117891 CAPLUS Full-text

DN 143:367597

TI Process for the preparation of perindopril

IN Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra

PA Neopharma Limited, UK

SO Brit. UK Pat. Appl., 21 pp.

CODEN: BAXXDU

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2413128	A	20051019	GB 2004-8258	20040413
AU 2005232938	A1	20051027	AU 2005-232938	20050407
CA 2562843	A1	20051027	CA 2005-2562843	20050407
WO 2005100317	A1	20051027	WO 2005-GB1355	20050407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BM, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1751107	A1	20070214	EP 2005-732439	20050407
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007532616	T	20071115	JP 2007-507836	20050407
IN 20060606462	A	20070831	IN 2006-DN6462	20061101
KR 2007054142	A	20070528	KR 2006-723684	20061113
US 2007185335	A1	20070809	US 2007-599918	20070409
PRAI GB 2004-8258	A	20040413		
WO 2005-GB1355	W	20050407		

OS CASREACT 143:367597; MARPAT 143:367597

AB A process for preparing perindopril or a pharmaceutically-acceptable salt comprises coupling a 4-halo-, 4-alkoxy- or 4-nitrobenzyl ester of (2S,3aS,7aS)-2-carboxyoctahydroindole with N-[(S)-1-carbethoxybutyl]-L-alanine (1) in the presence of DCC and HOBt, followed by catalytic hydrogenolysis. The starting ester was obtained from (S)-indoline-2-carboxylic acid by hydrogenation-esterification and 1 was obtained from

DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005097261	A1	20051020	WO 2005-US10927	20050330
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BM, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SE, SZ, TD, TG, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2565324	A1	20051020	CA 2005-2565324	20050330
US 2005261201	A1	20051124	US 2005-94339	20050330
EP 1735055	A1	20061227	EP 2005-733103	20050330
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007531769	T	20071110	JP 2007-506567	20050330
KR 2007010151	A	20070722	KR 2006-721482	20061017
PRAI US 2004-557466P	P	20040330		
WO 2005-US10927	W	20050330		

OS MARPAT 143:379815

AB The invention discloses a method for reducing C-reactive protein in a subject in need of treatment thereof, wherein the subject is at risk of having or the subject has already had a vascular event or suffering from an inflammatory disease or disorder. In one embodiment, the vascular event is a cardiovascular event (e.g., myocardial infarction). In another embodiment, the vascular event is a cerebrovascular event (e.g., stroke, transient ischemic attacks). In yet another embodiment the vascular event is a peripheral vascular event (e.g., intermittent claudication). The method comprises administering a therapeutically effective amount of at least one growth hormone secretagogue compound or a pharmaceutically acceptable salt, hydrate or solvate thereof. The growth hormone secretagogue can be coadministered with a second growth hormone secretagogue, HMG CoA reductase inhibitor, an ACAT inhibitor, a CETP inhibitor, an anti-inflammatory agent, an ACE inhibitor, a beta blocker, a cholesterol absorption inhibitor, a nicotinic acid, a fabric acid derivative, a bile acid sequestering agent or a combination thereof.

IT 82834-16-0, Perindopril

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(growth hormone secretagogues for reducing C-reactive protein, and use with other agents)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

norvaline Et ester and pyruvic acid under catalytic hydrogenation conditions. The method was applied to the synthesis perindopril erbumine (20.5 g obtained from 24 g 4-chlorobenzyl ester and 21.26 g l).

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril

erbumine

RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP

(Preparation)

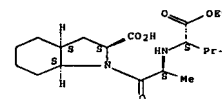
(preparation of perindopril by acylation of octahydroindolecarboxylates

with ethoxycarbonylbutylalanine)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

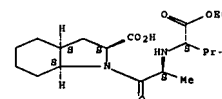
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

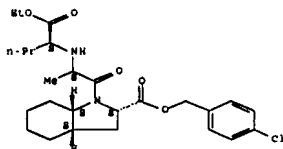
CRN 75-64-9

CMP C4 H11 N



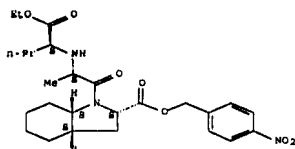
IT 41714 5- 6P 866310 04 9P
 RL RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation of perindopril by acylation of octahydroindolecarboxylates
 with
 ethoxycarbonylbutylalanine)
 RN 793716-56-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-
 (ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (4-
 chlorophenyl)methyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 866430-96-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-
 (ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (4-nitrophenyl)methyl
 ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

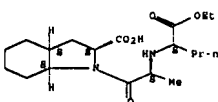
Absolute stereochemistry.



RE.CMT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT TGF-β2 gene mutation was associated with higher urinary TGF-β2
 level in hypertensive patient)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-
 (ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CMT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LB ANSWER 80 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM
 AN 2005:962026 CAPLUS Full-text
 DN 143:254016

TI Combination of (S)-amlodipine and an ACE inhibitor for reducing
 hypertension

IN Bush, Leroy; Orogan, Donna Roy
 PA Saprator 110 USA

SO PCT Int. Appl., 85 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CMT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005079772	A2	20050901	WO 2005-US4460	20050214
WO 2005079772	A3	20051103		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TW, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, NZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI US 2004-545451P P 20040218

US 2004-554030P P 20040318

US 2005-649633P P 20050203

AB The present invention generally relates to pharmaceutical compns. comprising optically pure (S)-amlodipine and an ACE inhibitor. In a preferred embodiment the (S)-amlodipine is (S)-amlodipine-L-malate, or a polymorph, pseudopolymorph or solvate thereof. In a preferred embodiment, the ACE inhibitor is ramipril. The pharmaceutical compns. of the invention are useful in the treatment of hypertension. The present invention also relates to a method of treating a

LB ANSWER 79 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM
 AN 2005:1107718 CAPLUS Full-text
 DN 144:148257

TI Role of transforming growth factor-β2 in, and a possible Transforming
 growth factor-β2 gene polymorphism as a marker of, renal
 dysfunction in essential hypertension: A study in turkish patients
 AU Bick, Zerrin; Gonen, Sevim; Bahcebas, Talat; Reis, Kadriye; Arinay, Turgay; Sindel, Sukru
 CS Department of Nephrology, Medical Faculty, Abant Izzet Baysal University, Duzce, Turk.
 SO Current Therapeutic Research (2006), 66(4), 266-278
 CODEN: CTCRA9; ISSN: 0011-393X
 PB Excerpta Medica, Inc.
 DT Journal
 LA English

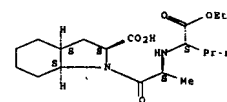
AB Background: Many studies have shown that transforming growth factor (TGF)-β has a major role in renal scarring in many renal diseases and hypertension. Objectives: The primary aim of this study was to investigate both the relationship between hypertension and serum and urinary levels of TGF-β2 (a more sensitive isoform for glomeruli than TGF-β1), and the effects of combination therapy with perindopril + indapamide on microalbuminuria, which becomes an early indicator of hypertensive benign nephropathy, and serum and urinary TGF-β2 levels in patients with mild to moderate essential hypertension. In addition, we examined the possible relationship between TGF-β2 gene polymorphism and essential hypertension. Methods: This study was conducted at the Department of Nephrol., Medical Faculty, Gazi University, Ankara, Turkey. Patients aged 218 years with newly diagnosed mild to moderate essential hypertension (systolic/diastolic blood pressure [SBP/DBP] >120/80 mm Hg) who had not previously received antihypertensive treatment were included in the study. Patients with stage I hypertension received perindopril 2 mg + indapamide 0.625 mg (tablet), and patients with stage II hypertension received perindopril 4 mg + indapamide 1.125 mg (tablet). All study drugs were given OD (morning) PO with food for 6 mo. Serum and urinary TGF-β2 and creatinine levels and serum and urinary albumin levels were measured before and after perindopril + indapamide administration. Amplified DNA fragments of the TGF-β2 primer region were screened using amplification refractory mutation system polymerase chain reaction anal., and the number of ACA repeats was confirmed by DNA sequencing. Genetic studies were performed using a com. TGF-β2 kit. Results: Forty patients were enrolled in the study, and 38 patients (27 women, 11 men; mean [SD] age, 46.3 [6.5] years) completed it. SBP and DBP were significantly decreased from baseline with perindopril/indapamide (both, P < 0.001). Microalbuminuria and urinary TGF-β2 levels also decreased significantly from baseline (P = 0.04 and P < 0.001, resp.), whereas the serum TGF-β2 level did not change significantly. Three patients, all of whom were found to have TGF-β2 gene mutations, had increased urinary TGF-β2 levels despite good blood pressure control. Conclusions: The results of this study in patients with mild to moderate hypertension suggest that, despite good clin. control of blood pressure, the persistence of microalbuminuria and high urinary TGF-β2 levels might predict renal impairment. When treating these patients, genetic tendencies and possible polymorphisms on the TGF-β2 locus should be kept in mind.

IT 82834-16-0, Perindopril
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (combined therapy of perindopril and indapamide reduced SBP and DBP, reduced microalbuminuria and urinary TGF-β2 but not of serum and

patient suffering from hypertension or a cardiac disorder, comprising co-administering a therapeutically effective amount of optically pure (S)-amlodipine and an ACE inhibitor. In a preferred embodiment the (S)-amlodipine is (S)-amlodipine-L-malate, or a polymorph, pseudopolymorph or solvate thereof. In a preferred embodiment, the ACE inhibitor is ramipril. The preparation and properties of (S)-amlodipine L-malate solvates and the polymorphs are given.

IT 82834-16-0, Perindopril
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Combination of amlodipine and ACE inhibitor for reducing hypertension)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-
 (ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (-).



LB ANSWER 81 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM
 AN 2005:729537 CAPLUS Full-text
 DN 143:211920

TI Preparation of diacylglycerol acyltransferase (DGAT1) inhibitors as
 anorectics

IN Ogawa, Nobuya; Okuma, Chihiro; Furukawa, Noboru

PA Japan Tobacco Inc.; Japan; Amgen Sf, LLC

SO PCT Int. Appl., 10 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CMT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005072740	A2	20050811	WO 2005-JP1643	20050128
WO 2005072740	A3	20051027		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, NZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2005209115	A1	20050811	AU 2005-209115	20050128
CA 2554455	A1	20050811	CA 2005-2554455	20050128
EP 1718309	A2	20061108	EP 2005-704403	20050128

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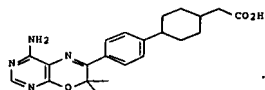
169 of 361

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

CN 1913899 A 20070214 CN 2005-80003524 20050128
JP 2007519605 T 20070719 JP 2006-524132 20050128
US 2007027093 A1 20070201 US 2006-495095 20060728
IN 2006CN03150 A 20070608 IN 2006-CN3150 20060830

PRAI JP 2004-24812 A 20040110
US 2004-598037P P 20040802
WO 2005-JP1643 W 20050128

OS CASREACT 143:211920; MARPAT 143:211920
GI



AB Claimed are anorectics comprising as active ingredients compds. having DGAT inhibitory activity (DGAT1 inhibitory activity) or a prodrugs or a pharmaceutically acceptable salts thereof. Thus, title compound (I) (preparation given) at 10 mg/kg orally in rats gave a 30% reduction in food consumption after 8 h.

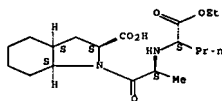
IT 107133-36-8, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of diacylglycerol acyltransferase (DGAT1) inhibitors as anorectics)

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



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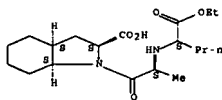
171 of 361

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

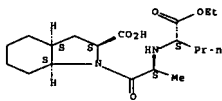
CRN 75-64-9
CMF C4 H11 N



IT 82834-16-0P, Perindopril
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril and perindopril erbumine)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



10576386

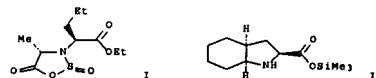
170 of 361

CM 2
CRN 75-64-9
CMF C4 H11 N



ANSWER 82 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
2005:698368 CAPLUS Full-text
DN 143:173145
TI Preparation of perindopril
IN Bhirud, Shekhar Bhaskar; Ahmed, Suhail; Chandrasekhar, Batchu; Durushotham, Vandanapu Loka Appala
PA Info
SO U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005171165	A1	20050809	US 2004-985097	20041110
PRAI IN 2003-MU1179	A	20031112		
US 2004-569041P	P	20040707		
OS CASREACT 143:173145				
GI				



AB A process for preparing a novel intermediate, oxathiazolidinedione I, in the preparation of perindopril is provided. Thus, reacting thionyl chloride in CH2Cl2 with imidazole and N-1(S)-(carboxyethyl)butyl-(S)-alanine gave I. Also provided are improved processes for the preparation of perindopril erbumine comprising (a) reacting I with a silylated octahydroindole-1H-2-carboxylic acid II to form perindopril, and (b) reacting perindopril with tert-butylamine to form perindopril erbumine.

IT 107133-36-8P
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril and perindopril erbumine)

RN 107133-36-8 CAPLUS

10576386

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ANSWER 83 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
2005:673315 CAPLUS Full-text
DN 143:159626
TI Inclusion complexes of perindopril
IN Rucman, Rudolf
PA LEK Pharmaceuticals D.O.O., Slovenia
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005068490	A1	20050728	WO 2005-EP282	20050113
W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SV, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: BM, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 21703	A	20050831	SI 2004-11	20040114
EP 1709066	A1	20061011	EP 2005-700892	20050113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
PRAI SI 2004-11	A	20040114		
WO 2005-EP282	W	20050113		

AB Complexes of the ACE-inhibitor perindopril, a salt, an addition salt or a derivative thereof with cyclodextrins, polyvinylpyrrolidone or hydroxypropyl cellulose, and processes for their preparation are described. E.g., complexes of perindopril erbumine with β -cyclodextrin and Me and hydroxypropyl β -cyclodextrins were prepared

IT 107133-36-8P, Perindopril erbumine, compds., with hydroxypropyl and Me cyclodextrins 860260-85-1P 860260-86-2P 860260-87-3P 860260-88-4P 860260-89-5P
RL: FRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inclusion complexes of perindopril)

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

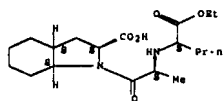
CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

10576386

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CM 2

CRN 75-64-9
CMF C4 H11 N

RN 860260-85-1 CAPLUS

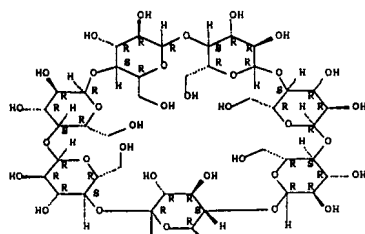
CN β -Cyclodextrin, compd. with 2-methyl-2-propanamine
(2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (9CI) (CA INDEX NAME)

CM 1

CRN 7585-39-9
CMF C42 H70 O35

Absolute stereochemistry.

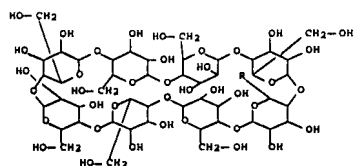
PAGE 1-A



10576386

175 of 361

CMF C48 H80 O40



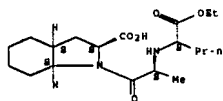
CM 2

CRN 107133-36-8
CMF C19 H32 N2 O5 . C4 H11 N

CM 3

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 4

CRN 75-64-9
CMF C4 H11 N

10576386

174 of 361



PAGE 2-A

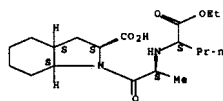
CM 2

CRN 107133-36-8
CMF C19 H32 N2 O5 . C4 H11 N

CM 3

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 4

CRN 75-64-9
CMF C4 H11 N

RN 860260-86-2 CAPLUS

CN γ -Cyclodextrin, compd. with 2-methyl-2-propanamine
(2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (9CI) (CA INDEX NAME)

CM 1

CRN 17465-86-0

10576386

176 of 361

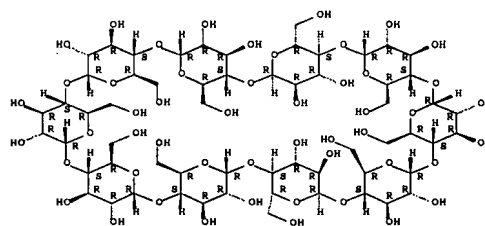
RN 860260-87-3 CAPLUS

CN ϵ -Cyclodextrin, compd. with 2-methyl-2-propanamine
(2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (9CI) (CA INDEX NAME)

CM 1

CRN 156510-98-4
CMF C60 H100 O50

Absolute stereochemistry.



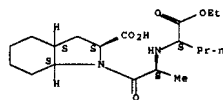
CM 2

CRN 107133-36-8
CMF C19 H32 N2 O5 . C4 H11 N

CM 3

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 4
CRN 75-64-9
CMF C4 H11 N



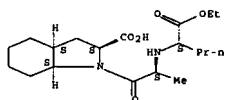
RN 860260-88-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 1-ethenyl-2-pyrrolidinone homopolymer and 2-methyl-2-propanamine (1:1:1) (9CI) (CA INDEX NAME)

CM 1
CRN 107133-36-8
CMF C19 H32 N2 O5 . C4 H11 N

CM 2

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 3
CRN 75-64-9
CMF C4 H11 N

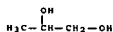


CM 4
CRN 9004-64-2
CMF C3 H8 O2 . x Unspecified

CM 5
CRN 9004-34-6
CMF Unspecified
CCI PMS, MAN

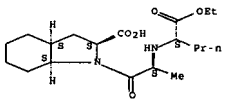
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 6
CRN 57-55-6
CMF C3 H8 O2



IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(inclusion complexes of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 107133-36-8, Perindopril erbumine
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(inclusion complexes of perindopril)

CM 4
CRN 9003-39-8
CMF (C6 H9 N O)x
CCI PMS

CM 5

CRN 88-12-0
CMF C6 H9 N O



RN 860260-89-5 CAPLUS
CN Cellulose, 2-hydroxypropyl ether, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid and 2-methyl-2-propanamine (7:1:1) (9CI) (CA INDEX NAME)

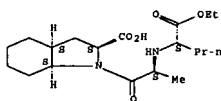
CM 1

CRN 107133-36-8
CMF C19 H32 N2 O5 . C4 H11 N

CM 2

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 3

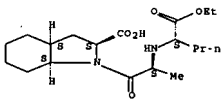
CRN 75-64-9
CMF C4 H11 N

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IP ANSWER 84 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AI 2005:673261 CAPLUS Full-text
DN 143:153713
TI New crystalline form of perindopril
IN Rucman, Rudolf
PA Lek Pharmaceuticals D. D., Slovenia
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005068425	A1	20050728	WO 2005-EP283	20050113

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI,

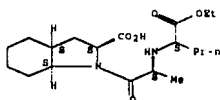
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 RW: BW, GH, GM, KE, LS, MM, MZ, NA, ND, NL, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VZ, VC, VN, YU, ZA, ZM, ZW
 SI 21704 A 20050831 SI 2004-12 20040114
 EP 1713771 A1 20041025 EP 2005-700693 20050113
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU
 PRAI SI 2004-12 A 20040114
 WO 2005-EP283 W 20050113

OS CASREACT 143:153713
 AB The invention relates to a process for the preparation of ACE inhibitor perindopril which starts from N-[(2S)-1-carboxybutyl]-L-alanine and involves trimethylsilyl protection and conversion to reactive acid chloride for reaction with (2S,3aS,7aS)-octahydroindole-2-carboxylic acid having a protected carboxyl group. The invention also relates to new crystalline and amorphous forms of perindopril. Thus, perindopril obtained by reaction of silylated reactants was purified by filtering a CH₂Cl₂ solution through a silica gel column and crystallizing from an Et ether solution. Perindopril in new crystalline form (78.2%) was obtained.

IT 82834-16-0P, Perindopril
 RI: IMP (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (Crystalline structure; preparation of perindopril in new crystalline form)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

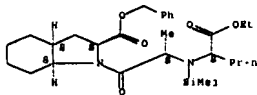


IT 107133-36-8P, Perindopril erbumine
 RI: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (preparation of perindopril in new crystalline form)

RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

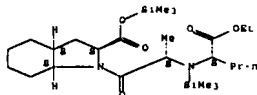
CM 1

CRN 82834-16-0



RN 861818-65-7 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, trimethylsilyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 85 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2005:436413 CAPLUS Full-text
 DN 143:139085

TI Effect of genetic variation on therapy with angiotensin converting enzyme inhibitors or angiotensin receptor blockers in dialysis patients
 AU Boeger, C. A.; Goets, A. K.; Krueger, B.; Hoesel, M.; Schmitz, G.; Riegler, G. A. J.; Kraemer, B. K.
 CS Klinik und Poliklinik fuer Innere Medizin II, University of Regensburg, Regensburg, Germany

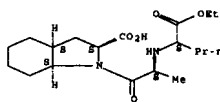
SO European Journal of Medical Research (2003), 10(4), 161-168
 CODEN: EJMRL; ISSN: 0949-2321

PB 1. Holsapfel Verlag GmbH
 DT Journal

LA English
 AB Introduction: The role of interaction of polymorphisms in the Renin-Angiotensin-System (RAS) with angiotensin converting enzyme (ACE) or angiotensin receptor (AGTR1) inhibitors (RAS inhibitors) is unknown, as is the role of such therapy in end stage renal disease (ESRD) patients. Methods: We enrolled all 445 prevalent patients with diabetic nephropathy receiving maintenance hemodialysis in 30 centers in Southern Germany from August 1999 to Jan. 2000 for prospective survival anal. until Dec. 2003. Blood pressure and medication was recorded at inclusion. We determined survival specific for allelic variants of the ACE (insertion/deletion), Angiotensinogen (M235T) and AGTR1 (A1166C) genes. The effect of therapy with RAS inhibitors at study inclusion was determined for the allelic variants of each gene. The primary end point was all cause mortality (ACM). Results: For all polymorphisms, and for therapy with RAS inhibitors there was no significant effect on survival in

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N

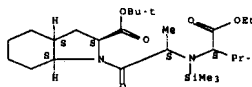


IT 859511-85-6P 861818-61-3P 861818-65-7P
 RI: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of perindopril in new crystalline form)

RN 859511-85-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 861818-61-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

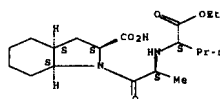
the complete collective (n = 445), though there was an insignificant trend for improved survival in patients on AGTR1 antagonists. Increased ACM risk was associated with treatment with RAS inhibitors only in patients homozygous for the wild type AGTR1 1166A allele (HR 1.65, p=0.01). For all other polymorphisms, therapy with RAS inhibitors had no significant effect on ACM, irrespectively of genotype. Similar results were obtained in patients with systolic ventricular dysfunction. Conclusion: Our data do not show a survival advantage for type 2 diabetes hemodialysis patients receiving RAS inhibiting therapy. In addition, our data indicate that allelic variation in RAS genes and pharmacogenetic interaction with RAS inhibition does not affect mortality risk in diabetic hemodialysis patients.

IT 82834-16-0, Perindopril
 RI: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (RAS inhibiting therapy with ACE inhibitors perindopril did not improve survival of diabetic nephropathy patient receiving maintenance hemodialysis)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 86 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 2005:436413 CAPLUS Full-text

DN 143:139085

TI Method for preparing N-carboxyalkyl dipeptide type angiotensin converting enzyme inhibitor

IN Shi, Huijun; Zhang, Qingwen; Zhong, Jingfen; Shan, Xiaoyan; Chen, Quoling; Zhou, Minghua

PA Shanghai Research Institute of Pharmaceutical Industry, Peop. Rep. China
 SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 11 pp.

CODEN: CNXXEV

DT Patent

LA Chinese

FAN.CNT 1

PATENT NO.	KIND	APPLICATION NO.	DATE
PI CN 1429835	A	20030716	20021230
PRAI CN 2002-139936		20021230	

AB The dipeptide, (I, R3OOC-CH(R1)NHCH(R2)CONR4R5 wherein R1 = Pr or phenethyl; R2 = Me, 4-trifluoroacetamidobutyl, or 4-aminobutyl; and R3 = H or ethyl), is prepared by allowing to react R3OOCCH(R1)NHCH(R2)CONH2 with bis(trichloromethyl) carbonate in solvent at (-20)-100°C for 1-50 h to obtain N-carboxylic

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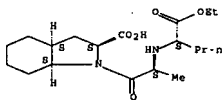
anhydride and then coupling with alpha-amino acid or its derivative in organic solvent at (-20)-100°C for 1-50 h. The alpha-amino acid or its derivative, R4R5NH, is 1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid benzyl ester, 2-azabicyclo[3.3.0]octane-3-carboxylic acid, 2-pyrrolidinecarboxylic acid, or octahydro-1H-indole-2-carboxylic acid.

IT 82834-16-0P, Perindopril
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (tert-butylamine salt; method for preparing N-carboxyalkyl dipeptide type angiotensin converting enzyme inhibitor)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LE ANSWER 87 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2005:412617 CAPLUS Full-text
 DN 143:90592

TI Insertion/deletion polymorphism of the ACE gene and adherence to ACE inhibitors

AU Schellerman, H.; Klungel, O. H.; van Duijn, C. M.; Witteman, J. C. M.; Hofman, A.; de Boer, A.; Stricker, B. H. Ch

CS Department of Epidemiology & Biostatistics, Erasmus MC, Rotterdam, Neth.

SO British Journal of Clinical Pharmacology (2005), 59(4), 483-485
 CODEN: BCPHEM; ISSN: 0306-5251

PB Blackwell Publishing Ltd.

DT Journal

LA English

AB We investigated whether the insertion/deletion (I/D) polymorphism of the ACE gene modified the adherence to ACE inhibitors as measured by the discontinuation of an ACE inhibitor, or addition of another antihypertensive drug. This was a cohort study among 239 subjects who started ACE inhibitor therapy. A Cox proportional hazard model was used to calculate relative risk (RR). During follow-up there was no significant difference between subjects with the DD, ID or II genotype (DD vs II; RR = 1.17, 95%CI: 0.78, 1.77 and ID vs II; RR = 1.06, 95%CI: 0.73, 1.55) in adherence. The I/D polymorphism of the ACE gene does not influence the adherence to ACE inhibitors.

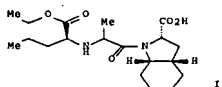
IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (ACE gene insertion/deletion polymorphism and adherence to ACE inhibitors)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-

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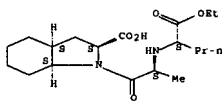
AB Crystalline perindopril erbumine (1.H2NBu-text) is prepared and the x-ray (powder) diffraction pattern given. The process comprises reacting a solution of perindopril (I), in a solvent selected from DMF or di-Me acetals of lower aliphatic aldehydes and ketones with tertiary butylamine and crystallization of the erbumine salt thus obtained by heating the reaction mixture to reflux, filtering hot, cooling gradually to 20-30°, and further cooling to 0-15° for 30 min-1 h and finally filtering off and drying the crystals.

IT 82834-16-0P, Perindopril
 RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of crystalline perindopril erbumine)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 107133-36-8P, Perindopril erbumine
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of crystalline perindopril erbumine)

RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

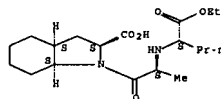
Absolute stereochemistry. Rotation (-).

10576386

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(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LE ANSWER 88 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2005:371219 CAPLUS Full-text
 DN 142:435775

TI Novel method for preparation of crystalline perindopril erbumine

IN Singh, Girij Pal; Godbole, Himanshu Madhav; Nehate, Sagar Purushottam

PA Lupin Ltd., India

SO PCT Int. Appl., 68 pp.
 CODEN: PIXXK2

DT Patent

LA English

FAN.CNT 1

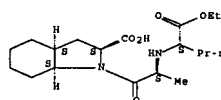
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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AU 2003300689	A1	20050505	AU 2003-300689	20031021
EP 1675827	A1	20060705	EP 2003-818870	20031021
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BR 2003018561	A	20061010	BR 2003-18561	20031021
JP 2007518668	T	20070712	JP 2005-509586	20031021
US 2007149604	A1	20070628	US 2006-576386	20060419
IN 2006MN00495	A	20070824	IN 2006-MN495	20060427
PRAI MO 2003-IN340	A	20031021		

GI

INSTANT

10576386

188 of 361



CM 2

CRN 75-64-9

CMF C4 H11 N

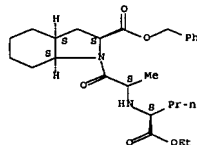


IT 122454-52-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of crystalline perindopril erbumine)

RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LE ANSWER 89 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2005:295060 CAPLUS Full-text
 DN 143:99536

TI Mortality in patients with hypertension on angiotensin-I converting enzyme

(ACE)-inhibitor treatment is influenced by the ACE insertion/deletion polymorphism.

AU Bleumink, Gyselle S.; Schut, Anna F. C.; Sturkenboom, Miriam C. J. M.; Van Duin, Cornelia M.; Deckers, Jaap W.; Holman, Albert; Kingma, J. Harre; Witteman, Jacqueline C. M.; Stricker, Bruno H. Ch.

CS Department of Epidemiology & Biostatistics, Erasmus Medical Center, Rotterdam, 3000 DR, Neth.

SO Pharmacogenetics and Genomics (2005), 15(2), 75-81

CODEN: PONEA1

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB The response to angiotensin-I converting enzyme (ACE)-inhibitor therapy is highly variable. Residual ACE activity during treatment, potentially modified by the ACE insertion/deletion (I/D) polymorphism, may explain part of this variability. We studied the possible interaction between ACE-inhibitor therapy in patients with hypertension and the ACE I/D polymorphism in incident heart failure and death. We studied 3365 hypertensive participants of the population-based Rotterdam Study, without heart failure at baseline for whom ACE-genotyping was successful. Incident heart failure was defined according to established criteria. In addition, total and cardiovascular mortality were studied as endpoints. A Cox regression model with use of ACE-inhibitors defined as time-dependent covariates was used for data-anal. Interaction was tested in this model assuming an allele-effect relationship. Although we could not demonstrate a beneficial effect of ACE-inhibitors, there was significant interaction between the ACE I/D polymorphism (II-ID-DD) and ACE-inhibitor use in the prediction of total and cardiovascular mortality. Mortality risk associated with treatment increased with the number of D alleles present; e.g. for total mortality in the II genotype group: RR=0.95 (95% CI 0.63-1.45), in the ID genotype group: RR=1.08 (95% CI 0.84-1.38) and in the DD genotype group: RR=1.61 (95% CI 1.18-2.18). No statistically significant interaction was found for incident heart failure. The results of our study suggest a relative resistance to ACE-inhibitor therapy in subjects with hypertension and the DD genotype compared to the II genotype, with the ID genotype in an intermediate position.

IT 82834-16-0, Perindopril

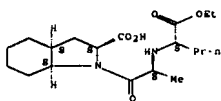
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ACE insertion/deletion influences mortality in hypertensive patients on ACE inhibitors)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CMT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 90 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM

142:296121 CAPLUS Full-text

TI Preparation of biphenyl or phenylheterocyclyl moiety-containing esters as inhibitors of microsomal triglyceride transfer protein

IN Hagiwara, Akio; Ikenogami, Taku; Mera, Yasuko; Sumida, Yukako; Iida, Akio; Tachibuchi, Toshio; Takahashi, Mitsuru

PA Japan Tobacco Inc., Japan

SO PCT Int. Appl., 229 pp.

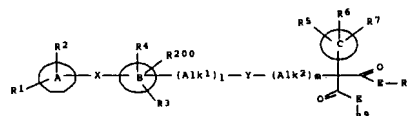
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CMT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005021486	A1	20050310	WO 2004-JP12407	20040827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SV, TJ, TM, TN, TR, TT, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, CH, CN, CO, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GM, GU, GW, ML, MR, NE, SN, TD, TG				
EP 1669345	A1	20060614	EP 2004-772363	20040827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2006205726	A1	20060914	US 2006-362375	20060227
PRAI JP 2003-305877	A	20030829		
WO 2004-JP12407	M	20040827		
OS MARPAT 142:298121				
GI				



AB The title compds. I (R1, R2 = H, alkyl, etc.; ring A = aryl, etc.; X = CO2(CH2)n, etc.; n = 0 - 3; R3, R4, R200 = H, halo, etc.; ring B = phenylene, etc.; ring C = Ph, etc.; R5, R6, R7 = H, alkyl, etc.; R8, R9 = H, (unsubstituted alkyl, etc.; E = O, etc.; Y = OCO, etc.; Alk1, Alk2 = alkanediyl, etc.; 1, m = 0 - 3) are prepared. Thus, di-ET 2-12-13-acetoxy-4-

(4'-trifluoromethylbiphenyl-2- carbonyl)amino]phenyl]acetoxymethyl)-2-phenylmalonate was prepared in 2 steps from di-ET 2-(2-(3-benzoyloxy-4-[(4'-trifluoromethylbiphenyl-2- carbonyl)amino]phenyl]acetoxymethyl)-2-phenylmalonate. In a test for the inhibition of triglyceride transfer activity between liposomes by microsomal triglyceride transfer protein, compds. of this invention showed IC50 values of < 10 nM to 1000 nM. Formulations are given.

IT 107132-36-8, Perindopril erbume

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination of biphenyl or phenylheterocyclyl moiety-containing esters (as inhibitors of microsomal triglyceride transfer protein) and α- and β-blockers)

RN 107132-36-8 CAPLUS

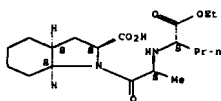
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N



RE.CMT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

LS ANSWER 91 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM

142:296121 CAPLUS Full-text

TI 2'-Benzothiazolylthioesters of N-substituted alpha amino acids: versatile intermediates for synthesis of ACE inhibitors

AU Singh, Girij Pal; Godbole, Himanshu M.; Nehate, Sagar P.; Mahajan, Pravin

R. Lupin Research Park, Lupin Ltd, Pune, India

SO Synthetic Communications (2005), 35(2), 243-248

CODEN: SYNCV; ISSN: 0039-7911

PB Taylor & Francis, Inc.

DT Journal

LA English

OS CASREACT 142:430514

AB ACE (angiotensin-converting enzyme) inhibitors have been synthesized in high diastereomeric selectivity by condensation of novel activated amino esters with cyclic amino acid esters using simple reaction conditions. The activated amino esters may be obtained from the corresponding carboxylic acids or their acid chlorides by activation with 2-mercapto-benzothiazole.

IT 122454-52-9P

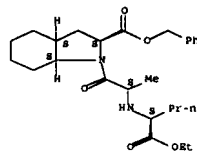
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(asym. synthesis of ACE inhibitors by condensation of mercaptobenzothiazole-activated esters with cyclic amino esters)

RN 122454-52-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



IT 82834-16-0P

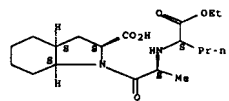
RL: SPN (Synthetic preparation); PREP (Preparation)

(asym. synthesis of ACE inhibitors by condensation of mercaptobenzothiazole-activated esters with cyclic amino esters)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

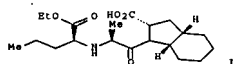
Absolute stereochemistry. Rotation (-).



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ ANSWER 92 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2005:182626 CAPLUS Full-text
DN 142:280052
TI Process for pure perindopril tert-butylamine salt
IN Parthasaradhi Reddy, Bandi; Rathnakar Reddy, Kura; Raji Reddy, Rapolu;
Muralidhara Reddy, Dasari; Ramakrishna Reddy, Matla
PA Hetero Drugs Pvt. Ltd., India
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

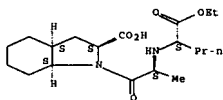
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005019173	A1	20050303	WO 2003-IN276	20030821
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RN: GH, GM, KE, LS, MN, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003263584	A1	20050310	AU 2003-263584	20030821
PRAI WO 2003-IN276	A1	20030821		
GI				



AB Pure perindopril tert-butylamine salt is obtained by extracting an aqueous solution of perindopril (I), namely (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid, or its salt contaminated with impurities with a suitable organic solvent such as methylene dichloride at a pH of 4.0 to 6.5, separating the organic layer, isolating I from the organic layer and converting it into tert-butylamine salt. Thus, perindopril tert-butylamine salt (15 g, purity 92.4%) was added to water (100 mL) and CH₂Cl₂ (100 mL) and the pH of the mass was adjusted to 5.4 by using 20% dilute HCl. The phases were separated and the aqueous layer was washed with CH₂Cl₂ (2 x 75 mL). The CH₂Cl₂ layer and washings are combined and the combined organic phase was washed with water (50 mL) and then with 10% aqueous NaCl (50 mL). The organic layer was dried over Na₂SO₄ and concentrated to give a residue, perindopril, (99.3 % purity). EtOAc (255 mL) was added to the residue (15 g) and stirred for 10 min to obtain a clear solution. Tert-Butylamine was added dropwise to the solution at 30° and stirred for 1 h at the same temperature. The reaction mass was then

CM 1
CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2
CRN 75-64-9
CMP C4 H11 N



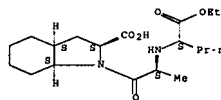
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ ANSWER 93 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2005:177840 CAPLUS Full-text
DN 142:274011
TI Nitrosated and nitrosylated cardiovascular compounds, their compositions, and use
IN Garvey, David S.; Letts, Gordon L.; Worcel, Manuel; Gaston, Ricky D.
PA Nitromed, Inc., USA
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005018561	A2	20050303	WO 2004-US26909	20040820
WO 2005018561	A3	20050721		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RN: BW, GH, GM, KE, LS, MN, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				

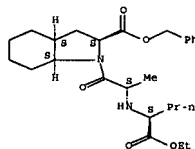
heated to reflux, passed over hifo rapidly at reflux temperature and washed with hot EtOAc (30 mL). Then, the reaction mass was stirred for 2 h at approx. 30°, cooled to 0°, and stirred for further 2 h at 0° to 5°. The separated solid was filtered, washed with EtOAc (15 mL), and dried to give 12 g of 99.77% pure perindopril tert-butylamine salt.
IT 82834-16-0P, Perindopril 122454-52-0P, (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid benzyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
RN (Intermediate; process for pure perindopril tert-butylamine salt)
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

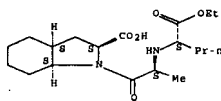


IT 107133-36-PP, Perindopril tert-butylamine salt
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
RN (process for pure perindopril tert-butylamine salt)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004266705	A1	20050303	AU 2004-266705	20040820
CA 2536173	A1	20050303	CA 2004-2536173	20040820
EP 1670459	A2	20060621	EP 2004-781569	20040820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007502831	T	20070215	JP 2006-524034	20040820
US 2007010571	A1	20070111	US 2006-569077	20060221
PRAI US 2003-496639P	P	20030820		
US 2003-496722P	P	20030820		
US 2003-496810P	P	20030821		
US 2003-498231P	P	20030828		
US 2003-498308P	P	20030828		
US 2003-530643P	P	20031219		
WO 2004-US26909	W	20040820		
OS MARPAT 142:274011				
AB Compns. and kits are described, comprising a nitrosated and/or nitrosylated cardiovascular compound, a nitric oxide donor compound and/or another therapeutic agent for treating cardiovascular diseases, renovascular diseases, diabetes, diseases resulting from oxidative stress, endothelial dysfunctions, diseases caused by endothelial dysfunctions, cirrhosis, pre-eclampsia, osteoporosis, and nephropathy. The nitrosated and/or nitrosylated cardiovascular compds. are preferably β -adrenergic antagonists, ACE inhibitors, anti-hyperlipidemic compds., or antithrombotic and vasodilator compds.				
IT 82834-16-0D, Perindopril, nitrosated and nitrosylated derivs. RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (nitrosated and nitrosylated cardiovascular compds., their compns., and use)				
RN 82834-16-0 CAPLUS				
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)				

Absolute stereochemistry. Rotation (-).



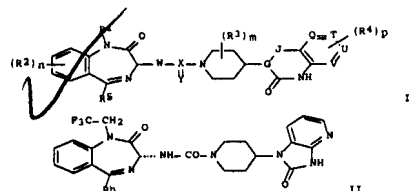
✓ ANSWER 94 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2005:136493 CAPLUS Full-text
DN 142:240471
TI Preparation of benzodiazepine derivatives as CGRP receptor antagonists
IN Burgey, Christopher S.; Stump, Craig A.; Williams, Theresa M.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2

10576386

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DT Patent
LA English
FAN.CNT 1

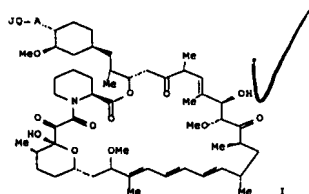
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005013894	A2	20050217	WO 2004-092029	20040624
WO 2005013894	A3	20060302		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, OA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004263080	A1	20050217	AU 2004-263080	20040624
CA 2529196	A1	20050217	CA 2004-2529196	20040624
EP 1641423	A2	20060405	EP 2004-776997	20040624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1842526	A	20061004	CN 2004-80017996	20040624
JP 2007516183	T	20070621	JP 2006-517599	20040624
US 2006135511	A1	20060622	US 2005-562297	20051222
PRAI US 2003-482854P	P	20030626		
WO 2004-092029	W	20040624		
OS CASREACT 142:240471; MARPAT 142:240471				
GI				



AB Benzodiazepine derivs. of formula I [R1 = H, alkyl, cycloalkyl, aryl, etc.; R2 = H, alkyl, cycloalkyl, aryl, etc.; R3 = H, alkyl, CO2H, alkoxy carbonyl; R4 = H, alkyl, cycloalkyl, aryl, etc.; R5 = H, alkyl, cycloalkyl, etc.; n = 1-4; m = 1-9; p = 1-4; W = O, (substituted) NH, (substituted) CH2; X = C, S; Y = O, NCONH2, etc.; Q, J = N, NCH2, etc.; Q, T, U, V = CH, N, with proviso] are prepared as antagonists of CGRP receptors, and are useful in the treatment or prevention of diseases in which the CGRP is involved, such as headache, migraine and cluster headache. The invention is also directed to

10576386

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US 2006-494418 A1 20060727
OS CASREACT 142:219083; MARPAT 142:219083
GI

AB Rapamycin derivs. containing phosphorus moiety, such as I [A = O, S, NR2, absent; Q = V, OV, SV, NR2, absent; V = aliphatic, heteroaliph., aryl, heteroaryl moiety, such that J is linked to the cyclohexyl ring directly, through A or through VA, OVA, SVA or NR2VA; J = P(K)(YR5)2, P(YR5)2, P(K)(YR5)OR6; K = O, S; Y = O, S, NR2, bond; R2, R5 = aliphatic, heteroaliph., aryl, heteroaryl, H; R6 = PK(YR5)YR5, SO2YR5, C(O)YR5; G = O, S, NR2, (M)X; M = (un)substituted methylene, alkyl, alkylene; X = 1-6], and pharmaceutically acceptable derivs. thereof, were prepared for therapeutic use as immunosuppressive and anticancer agents. These rapamycin derivs. are useful for treatment of graft vs. host disease, lupus, rheumatoid arthritis, diabetes mellitus, myasthenia gravis, multiple sclerosis, psoriasis, dermatitis, eczema, seborrhea, inflammatory bowel disease, pulmonary inflammation, ocular uveitis; adult T-cell leukemia, lymphoma, fungal infections, hyperproliferative retinosis, graft vascular atherosclerosis, coronary artery disease, cerebrovascular disease, arteriosclerosis, atherosclerosis, nonatheromatous arteriosclerosis, or vascular wall damage from cellular events leading toward immune mediated vascular damage, stroke or multi-infarct dementia. Thus, I [A-QS = OP(O)(OBu)Me] was prepared by reacting rapamycin with methylphosphonic dichloride and n-butanol using 3,5-tlutidine in CH2Cl2 under a nitrogen atmosphere. Binding affinity of the rapamycin phosphorus derivs. for human FKBP-12 protein was assayed, dosages for retinosis prevention were discussed.

IT 22834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. as immunosuppressive and anticancer agents)

RN 22834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

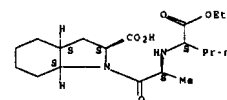
10576386

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pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which CGRP is involved. Thus, II was prepared in several steps. The prepared compd. had IC50 values < 50 μM against CGRP receptor.

IT 22834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agent for co-administration with benzodiazepines)
RN 22834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



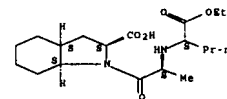
✓ ANSWER 95 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM

AI 2005122803 CAPLUS Full-text
DN 142:219083
TI Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as immunosuppressive and anticancer agents
IN Metcalf, Chester A., III; Rozamus, Leonard W.; Wang, Yihan; Berstein, David L.
PA Ariad Gene Therapeutics, Inc., USA
SO U.S. Pat. Appl. Publ., 57 pp., Cont.-in-part of U.S. Ser. No. 635,054.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005032825	A1	20050210	US 2004-862149	20040604
US 7091213	B2	20060815		
US 2003220297	A1	20031127	US 2003-357152	20030203
US 2004073024	A1	20040415	US 2002-635054	20030806
US 2006264405	A1	20061123	US 2006-429582	20060505
US 2006264456	A1	20061123	US 2006-494418	20060727
US 7186826	B2	20070306		
US 2007190106	A1	20070816	US 2007-650017	20070105
PRAI US 2002-353252P	P	20020201		
US 2002-426928P	P	20021115		
US 2002-428383P	P	20021122		
US 2002-433930P	P	20021217		
US 2003-357152	A2	20030203		
US 2003-635054	A2	20030806		
US 2003-486367P	P	20030711		
US 2004-862149	A2	20040604		
US 2004-869163	B2	20040712		
US 2005-711859P	P	20050826		

10576386

200 of 361

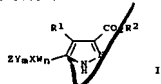


RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ ANSWER 96 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM

AI 2005120729 CAPLUS Full-text
DN 142:219276
TI Preparation of 5-substituted 2H-pyrazole-3-carboxylic acid derivatives as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases
IN Semple, Graeme; Gharabadi, Tawfik; Shin, Young-Jun; Decaire, Marc; Averbu, Claudie; Skinner, Philip J.
PA Arena Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

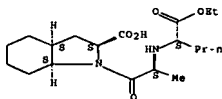
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005011677	A1	20050210	WO 2004-081839	20040610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, OA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004260636	A1	20050210	AU 2004-260636	20040610
CA 2528834	A1	20050210	CA 2004-2528834	20040610
EP 1633351	A1	20060315	EP 2004-776418	20040610
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007032537	A1	20070208	US 2006-560332	20060908
PRAI US 2003-478644P	P	20030613		
WO 2004-081839	W	20040610		
OS MARPAT 142:219276				
GI				



AB Title compds. [I; W, Y = (substituted) alkylene, alkenylene, alkynylene; X = NR3CO, NR3SO2, NR3, CO, CH(OH), C(NH), O, S, SO, SO2, etc.; R3, R4 = H, (substituted) alkyl, Ph, heteroaryl; Z = H, halo, (substituted) Ph, heteroaryl; R1 = H, OH, halo, alkyl, haloalkyl; R2 = H, alkyl; m, n = 0, 1; with proviso(s)], were prepared. Thus, 5-methylthiomethyl-2H-pyrazole-3-carboxylic acid (preparation outlined) showed hRUP25 agonist activity with EC50 = 4.3 µM.

IT 82834-16-0, Perindopril
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (coadministration; preparation of pyrazolecarboxylates as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 97 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2005:99521 CAPLUS Full-text
 DN 142:156329

TI Preparation of α-amino acid benzothiazolylthio esters as intermediates for manufacture of ACE inhibitors
 IN Singh, Girij Pal; Godbole, Himanshu Madhav; Mahajan, Pravin Raghunath; Nehate, Sagar Purushottam
 PA Lupin Limited, India
 SO PCT Int. Appl., 108 pp.
 CODEN: PIXXD2
 DT Patent
 LA English

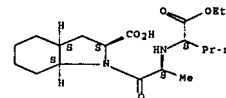
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005010028	A1	20050203	WO 2003-IN257	20030731

 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2003272077 A1 20050214 AU 2003-272077 20030731
 PRAI WO 2003-IN257 A 20030731
 OS CASREACT 142:156329; MARPAT 142:156329
 AB The invention relates to esters (S,S)-RCH2CH2CH(CO2R1)NHCHR2CO-X (I; R is alkyl or Ph; R1 H or alkyl; R2 is alkyl or aminoalkyl; X is 2-benzothiazolylthio) which are intermediates in the manufacture of ACE inhibitors I (X is an amino acid or derivative). The intermediate benzothiazolylthio esters were prepared by reaction of the appropriate acid or acid chloride with 2,2'-dithiobis(benzothiazole) or 2-mercaptobenzothiazole. Thus, treatment of N-[(1S)-(ethoxycarbonyl)-3-phenylpropyl]-N6-(trifluoroacetyl)-L-lysine (preparation given) with 2,2'-dithiobis(benzothiazole), followed by coupling with L-proline Et ester and deprotection, afforded lisinopril dihydrate.
 IT 82834-16-0P, Perindopril 197133-36-8P, Perindopril erbumine
 RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of α-amino acid benzothiazolylthio esters as intermediates for manufacture of ACE inhibitors)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

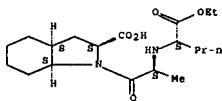


RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



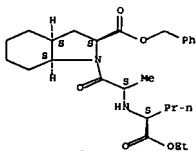
CM 2

CRN 75-64-9
 CMF C4 H11 N



IT 122454-52-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of α-amino acid benzothiazolylthio esters as intermediates for manufacture of ACE inhibitors)
 RN 122454-52-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 98 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2005:50771 CAPLUS Full-text
 DN 142:107409

TI The use of inhibitors of the renin-angiotensin system for the prevention and treatment of stroke
 IN Montgomery, Hugh Edward; Martin, John Francis; Erusalimsky, Jorge Daniel
 PA Ark Therapeutics Limited, UK; Boehringer Ingelheim International GmbH
 SO Eur. Pat. Appl., 17 pp.
 CODEN: EPAXDW
 DT Patent
 LA English

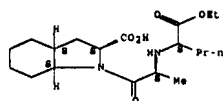
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1498124	A2	20050119	EP 2004-21889	19981019
EP 1498124	A3	20050817		
EP 1498124	B1	20070704		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
EP 1023067	A2	20000802	EP 1998-947698	19981019
EP 1023067	B1	20050504		
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1123342	B	20031008	CN 1998-811314	19981019
EP 1559424	A2	20050803	EP 2005-9398	19981019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
ES 2238770	T3	20050901	ES 1998-947698	19981019
EP 1776954	A2	20070425	EP 2007-102160	19981019
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, AL, BA, HR, MK, YU				
AT 366110	T	20070715	AT 2004-21889	19981019
PRAI GB 1997-22026	A	19971017		
GB 1998-10855	A	19980520		
EP 1998-947698	A3	19981019		
US 1997-67819P	P	19971205		
US 1998-94902P	P	19980731		
EP 2004-21889	A3	19981019		
WO 1998-031322	M	19981019		

AB An inhibitor of the renin-angiotensin system is used for the manufacture of a medicament for the treatment or prevention of stroke or its recurrence. The inhibitor is selected from quinapril, captopril, lisinopril, perindopril, trandolapril, enalapril, moexipril, fosinopril, ramipril, cilazapril, imidapril, spirapril, temocapril, benazepril, alacepril, ceronapril, delapril, moxetipril, trandolapril, losartan, valsartan, irbesartan, candesartan, eprosartan, tasosartan and telmisartan.

IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (renin-angiotensin system inhibitors for prevention and treatment of stroke)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



✓ ANSWER 99 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM
AN 2005:43552 CAPLUS Full-text
DN 142:259096

TI Effects of perindopril treatment on hemostatic function in patients with essential hypertension in relation to angiotensin converting enzyme (ACE) and plasminogen activator inhibitor-1 (PAI-1) gene polymorphisms
AU Jastrzebska, M.; Wieducka, K.; Narusiewicz, M.; Ciechanowicz, A.; Jancsak-Basari, A.; Polynska, A.; Goracy, I.; Chetkowski, K.; Wesotowska, T.

CS Chair of Clinical Biochemistry, Pomeranian Medical University, Szczecin, Pol.

SO Nutrition, Metabolism and Cardiovascular Diseases (2004), 14(5), 259-269
CODEN: NMCDEE; ISSN: 0939-4753

PS Medikal Press

DT Journal

LA English

AB An imbalance in the hemostatic system is a frequent finding in untreated essential hypertension (HT), and it has been shown that treatment with angiotensin converting enzyme (ACE) inhibitors improves hemostatic function. In order to elucidate the role of genetic factors, we studied hemostasis in patients with untreated and treated HT and correlated the results with ACE I/D and plasminogen activator inhibitor-1 (PAI-1) 4G/5G gene polymorphisms. Forty-three males with HT (mean age 51.7±6.8 years) were compared with 34 age and gender-matched controls. All of the patients were treated with perindopril (4 mg/day) and, after one and six months of therapy, their levels of plasma fibrinogen (Fb), t-PA antigen, PAI-1 antigen, von Willebrand factor (vWF), ACE activity and blood pressure were measured. ACE and PAI-1 genotypes were identified by means of the polymerase chain reaction on DNA isolated from peripheral blood lymphocytes. Untreated patients had significantly higher levels of Fb, PAI-1 (p<0.01) and t-PA (p<0.05) regardless of their ACE or PAI-1 genotypes. Perindopril reduced blood pressure regardless of ACE or PAI-1 genotype (p<0.001). ACE II homozygotes showed the greatest decrease in ACE activity (p<0.01) and a significant reduction in Fb levels (p<0.05) after just one month of treatment. Anal. of the group as a whole revealed an increase in t-PA antigen levels after six months of treatment, regardless of ACE or PAI-1 genotype (p<0.01). Our results show that essential hypertension predisposes to the procoagulant state characterized by hyperfibrinogenemia and hypofibrinolysis. Perindopril reduced fibrinogen levels in ACE II homozygotes due to its more potent inhibitory action on the renin-angiotensin system in such patients. It improved fibrinolysis by increasing t-PA levels regardless of ACE and PAI-1 genotype.

IT 82834-16-0, Perindopril

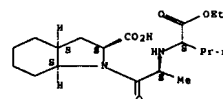
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(perindopril reduced fibrinogen levels by inhibiting renin-angiotensin system in ACE II homozygotic hypertensive patient, increased t-PA levels thus improved fibrinolysis in hypertensive patient regardless of

ACE or PAI-1 genotype)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 43 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ ANSWER 100 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2005:33235 CAPLUS Full-text

DN 142:128576

TI Detection of SNPs in human carboxyl esterase I gene for evaluation of drug metabolism

IM J1, Guli-Jing, Muramatsu, Masaaki, Katagiri, Takashi, Shimotsukasa, Eiichi

PA Huhit Genomix Inc., Japan

SO Jpn. Kokai Tokkyo Koho, 144 pp.

CODEN: JXXXXF

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2005006572	A	20050113	JP 2003-175498	20030619
PRAI JP 2003-175498				

AB This invention provides a process of detection of SNPs in human carboxyl esterase I gene. The DNA sequence for human carboxyl esterase I were disclosed. The SNPs occur at both promoter region and coding region of carboxyl esterase I gene. The method provided in this invention can be used for evaluation of angiotensin converting enzyme inhibitor metabolism in patients of hypertension, diabetic renal failure, cardiac insufficiency and juvenile pneumonia.

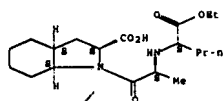
IT 82834-16-0, Perindopril

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor of, metabolism of; detection of SNPs in human carboxyl esterase I gene for evaluation of drug metabolism)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



✓ ANSWER 101 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2005:14369 CAPLUS Full-text

DN 142:114110

TI Preparation of benzodiazepine CGRP receptor antagonists

IN Burgey, Christopher S.; Stump, Craig A.; Williams, Theresa M.

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005000807	A2	20050106	WO 2004-US20206	20040624
WO 2005000807	A3	20060105		

M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GR, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RM: BW, GH, GM, KE, LS, MM, MZ, NA, SD, SI, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, EG, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BP, BJ, CF, CG, CI, CM, OA, GN, GQ, GW, ML, MR, NE, SN, TD, TO

AU 2004252150 A1 20050106 AU 2004-252150 20040624

CA 2529227 A1 20050106 CA 2004-2529227 20040624

EP 1641781 A2 20060405 EP 2004-776996 20040624

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

CN 1812982 A 20060802 CN 2004-80017952 20040624

JP 2007516182 T 20070621 JP 2006-517597 20040624

US 2006148790 A1 20060706 US 2005-562298 20051222

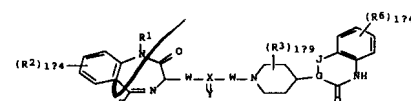
US 7196079 B2 20070327 20040624

PRAI US 2003-482674P P 20030626 20040624

WO 2004-US20206 W 20040624

CS CASREACT 142:114110; MARPAT 142:114110

DI



AB Title compds. I (R1 = H, alk(en/yn)yl, etc.; R2 = H, alkyl, cycloalkyl, etc.; R3 = H, alk(en/yn)yl, etc.; W = O, amino, alkyl; X = C, S; Y = O, NCN, etc.; R4 = H, alkyl, CN, etc.; R5 = H, alkyl, cycloalkyl, etc.; G-J = N, N-alkyl, etc.) are prepared for instance, II is prepared from (R)-3-amino-1-ethyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepine oxalate, p-nitrophenylchloroformate and 3-(piperidin-4-yl)-3,4-dihydroquinazolin-2(1H)-one hydrochloride. Compds. I exhibit affinity for the CGRP receptor with an IC50 of less than 50µM. I, alone or in combination with other agents, are useful for the treatment of diseases in which the CGRP is involved, such as headache, migraine and cluster headache.

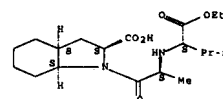
IT 82834-16-0, Perindopril

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of benzodiazepine CGRP receptor antagonists for headaches)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



✓ ANSWER 102 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2004:1154670 CAPLUS Full-text

DN 142:62765

10576386

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TI Preparation of various crystalline forms of perindopril erburbine for use as drug

IN Straessler, Christoph; Lelek, Vit; Faessler, Roger

PA Azad Pharmaceutical Ingredients AG, Switz.

SO PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004/13293	A1	20041229	WO 2004-CH374	20040618
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2530550	A1	20041208	CA 2004-2530550	20040618
AU 2004249345	A1	20041229	AU 2004-249345	20040618
EP 1636185	A1	20060322	EP 2004-737029	20040618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1812971	A	20060802	CN 2004-80017867	20040618
BR 2004011966	A	20060829	BR 2004-11966	20040618
JP 200707418	T	20070329	JP 2006-515624	20040618
MX 2005PA13811	A	20060627	MX 2005-PA13811	20051216
NO 2006000256	A	20060118	NO 2006-256	20060118
US 2007135512	A1	20070614	US 2006-560464	20061128
PRAI CH 2003-1109	A	20030624		
WO 2004-CH374	N	20040618		

AB Disclosed are two novel crystalline forms d and e of perindopril erburbine, which are suitable as therapeutic substances in medicaments used for treating cardiovascular diseases, especially high blood pressure and cardiac insufficiency. Crystalline form e is obtained by crystallizing perindopril erburbine from MTBE containing 1.5 to 2.5 % (volume/volume) of water at 30 to 45°, preferably 34 to 45°, crystallization expediently taking place by stirring. Crystalline form e changes into crystalline form d if the water is removed, practically by azeotropic distillation, preferably at 35 to 37°, and stirring continues for at least 15 h at 30 to 45°, preferably 35 to 37°. Crystalline form d can also be obtained by stirring crystalline form a or ss in tert-Bu Me ether containing 0.9 to 1.4 % (volume/volume) of water at 33 to 38° while inoculating the same with crystalline form d. Crystalline form e can further be obtained by stirring crystalline form a or ss in tert-Bu Me ether containing 0.9 to 1.4 % (volume/volume) of water at 28 to 35° while inoculating the same with crystalline form e, or by stirring crystalline form a or ss in tert-Bu Me ether containing 1.5 to 2.0 % (volume/volume) of water at 35 to 38°.

IT 107133-36-S, Perindopril erburbine
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(preparation of various crystalline forms of perindopril erburbine for use as drug)

RN 107133-36-8 CAPLUS

10576386

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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 21507	A	20041231	SI 2003-123	20030516
EP 1628956	A1	20060301	EP 2004-731808	20040507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007072919	A1	20070329	US 2006-556986	20060929
PRAI SI 2003-123	A	20030516		
NO 2004-S121	N	20040507		

OS MARPAT 141:424441

AB The invention relates to a process for the preparation of ACE-inhibitory peptides (S,S)-R1CH2CH2CH(CO2R2)-L-Ala-NR3R4 (R1 is H, alkyl, phenyl; R2 is H, alkyl; NR3R4 is a proline, 2-piperidinecarboxylic or hexahydro-2-azepinecarboxylic acid residue and related aza/thia analogs and their esters or metal salts) in which the carboxy group of (S,S)-R1CH2CH2CH(CO2R2)-L-Ala-OH is activated with a uronium salt in an aprotic solvent prior to coupling with an amino acid HNR3R4. Thus, a mixture of N-(1(S)-(ethoxycarbonyl)-3-phenylpropyl)-L-alanine, L-proline, Et3N and O-(benzotriazol-1-yl)-N,N,N'-tetramethyluronium hexafluorophosphate in acetonitrile-DMF was stirred for 30 min at room temperature to afford enalapril (85.4% yield of maleate).

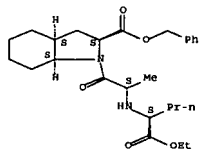
IT 122454-E2-8P
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PKEP (Preparation)

(preparation of enalapril maleate and related compds. having ACE inhibitory action)

RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LA ANSWER 104 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2004:1009942 CAPLUS Full-text

DN 141:292431

TI Test kit, method and software for evaluating the pharmacodynamic effect of ACEI-like antihypertensive agent and its compounded medicine

10576386

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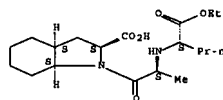
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LA ANSWER 103 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2004:1016010 CAPLUS Full-text

DN 141:424441

TI Process for the preparation of enalapril maleate and related compounds having ACE inhibitory action

IN Jenko, Branko

PA Lek Pharmaceuticals D.D., Slovenia

SO PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004/151515	A1	20041125	WO 2004-S121	20040507
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				

10576386

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IN King, Houkun; Jiang, Shanqun; Zhu, Guoying; Zhang, Minmin; Yu, Yunxian; Guang, Wenwei; Hong, Xiumei; Chen, Changzhong; Chen, Guangliang

PA Anhui Institute of Biomedicine, Peop. Rep. China

SO Faming Zhuanli, Henqing Gongkai Shixingshu, 23 pp.

CODEN: CNXKEV

DT Patent

LA Chinese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1472337	A	20040204	CN 2002-125863	20020731
CN 1679943	A	20051012	CN 2005-1008999	20020731
PRAI CN 2002-125863	A3	20020731		

AB The test kit consists of a pair of primers, endonuclease Hae III and its buffer II, PCR buffer, DNA polymerase Taq, and dNTPs. The PCR buffer is composed of KCl, Tris-HCl, and MgCl2. The buffer II is composed of Tris-HCl, MgCl2, NaCl, and DTT. The pharmacodynamic effect of ACEI-like antihypertensive agents is evaluated by using the test kit to analyze the genotype of polymorphic locus Ag919Gly of MS gene of homocysteine metabolic pathway. The software for evaluating the pharmacodynamic effect of ACEI-like antihypertensive agent is designed based on the genotype of MS gene, age, body mass, sex, height, basic diastolic pressure, basic systolic pressure, smoking history, etc. The compounded medicine for improving the pharmacodynamic effect of ACEI-like antihypertensive agent is composed of ACEI-like antihypertensive agent and synergist. The ACEI-like antihypertensive agent is captopril, enalapril, cilazapril, benazepril, perindopril, ramipril, fosinopril, and/or lisinopril. The synergist is folic acid, tetrahydrofolic acid, vitamin B12, vitamin B6, and/or their compounded preparation

IT 82834-16-0, Perindopril

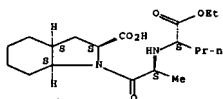
RL: ANT (Analyte); ANST (Analytical study)

(test kit, method and software for evaluating pharmacodynamic effect of ACEI-like antihypertensive agent and its compounded medicine)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LA ANSWER 105 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2004:996205 CAPLUS Full-text

DN 141:395815

TI A process for the preparation of perindopril using tetramethyluronium salts as coupling reagents

IN Rucman, Rudolf

PA Lek Pharmaceuticals D.D., Slovenia

SO PCT Int. Appl., 15 pp.

CODEN: PIXX02

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004099138	A1	20041118	WO 2004-8120	20040507
WI	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW	BW, GH, GM, KE, LS, MM, MZ, NA, SD, SI, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO			

SI 21506	A	20041231	SI 2003-118	20030508
EP 1628995	A1	20060301	EP 2004-731809	20040507
EP 1628995	B1	20070627		

R1	AT, BE, CN, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK			
AT 365748	T	20070715	AT 2004-731809	20040507
US 2007173637	A1	20070726	US 2006-555848	20061026

PRAI SI 2003-118	A	20030508		
WO 2004-8120	W	20040507		

OS CASREACT 141:395815; MARPAT 141:395815

AB A process for the preparation of the ACE inhibitor perindopril involves activation of N-[(S)-(ethoxycarbonyl)butyl]-L-alanine (I) with a tetramethyluronium salt in the presence of a tertiary organic base, coupling with (2S,3aS,7aS)-octahydroindole-2-carboxylic acid (2) or an ester, and deprotection. Thus, a mixture of 1, 2 benzyl ester, TBTU and diisopropylethylamine in DMF/CH₂Cl₂ was stirred for 4 h to afford benzyl-perindopril, which was converted to perindopril by phase transfer or classical hydrogenation.

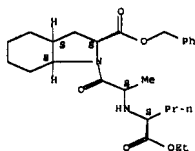
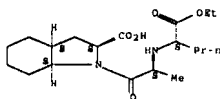
IT #244-16-UP, Perindopril

RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril using tetramethyluronium salts as coupling reagents)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LE ANSWER 106 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 0004:996123 CAPLUS Full-text

DN 141:411226

TI Process for preparation of perindopril and its salts

IN Kankar, Rajendra Naayanrao; Rao, Dharmaraj Ramachandra

PA Cipla Limited, 100/1, Main, Christopher Paul

SO PCT Int. Appl., 26 pp.

CODEN: PIXX02

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004099138	A2	20041118	WO 2004-GB2029	20040512
WO 2004099138	A3	20041223		
WI	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW	BW, GH, GM, KE, LS, MM, MZ, NA, SD, SI, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO			

IN 2003MU0468	A	20050211	IN 2003-MU468	20030512
PRAI IN 2003-MU468	A	20030512		

OS CASREACT 141:411226; MARPAT 141:411226

AB A process for preparing perindopril or a pharmaceutically-acceptable salt comprises esterifying (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid (I) with benzyl alc. (or the 4-chloro or 4-alkoxy derivative) in the presence of benzenesulfonic acid as catalyst, treating the intermediate ester benzenesulfonate with N-[(S)-1-carbomethoxybutyl]-L-alanine (II), and ester cleavage. Thus, 1 benzyl ester benzenesulfonate (40 g) was prepared, its suspension in CH₂Cl₂ made alkaline with aqueous ammonia, and the organic layer separated. Treatment with II at 10-15 °C in the presence of hydroxybenzotriazole and N,N'-dicyclohexylcarbodiimide and workup afforded 43 g perindopril benzyl ester.

IT #2834-16-UP, Perindopril 107133-36-8P, Perindopril

erbumine
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP

IT 107133-36-8P, Perindopril erbumine

RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP

(Preparation)

(preparation of perindopril using tetramethyluronium salts as coupling reagents)

RN 107133-36-8 CAPLUS

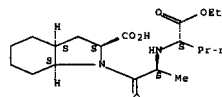
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



IT 122454-52-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(preparation of perindopril using tetramethyluronium salts as coupling reagents)

RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

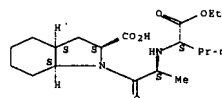
(Preparation)

(preparation of perindopril and its salts)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

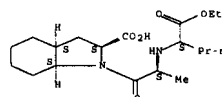
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1 *

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

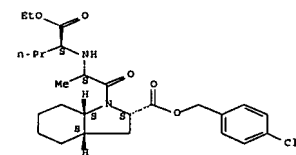
CMF C4 H11 N



IT 793716-56-0 793716-57-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of perindopril and its salts)
RN 793716-56-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (4-chlorophenyl)methyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

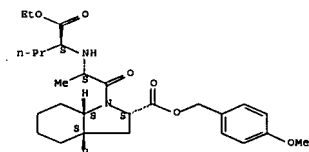
Absolute stereochemistry.



RN 793716-57-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (4-methoxyphenyl)methyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 122454-52-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril and its salts)

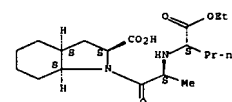
RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

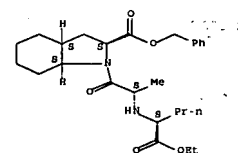
polymorphism)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 108 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2004-799452 CAPLUS Full-text
DN 141:301435
TI Acidic drug complexes for improved bioavailability and delivery
IN Yu, Ruey J.; Van Scott, Eugene J.
PA USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CMT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004082628	A2	20040930	WO 2004-US8112	20040317
WO 2004082628	A3	20041119		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RN:	BW, GH, GM, KE, LS, MW, MZ, SD, SE, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GW, GM, ML, MR, NE, NG, TD, TG			
US 2004222064	A1	20041104	US 2004-801134	20040316
AU 2004222305	A1	20040930	AU 2004-222305	20040317
CA 2519126	A1	20040930	CA 2004-2519126	20040317
EP 1603449	A2	20051214	EP 2004-757550	20040317
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK			
PRAI US 2003-454631P	P	20030317		
US 2004-801134	A	20040316		
WO 2004-US8112	A	20040317		
OS MARPAT 141:301435				
AB	Embodiments of the invention relate to a composition, a process of making the composition, and to the use of the composition. The comps. include a mol. complex formed between an acidic pharmaceutical drug and at least one			



L8 ANSWER 107 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2004-798985 CAPLUS Full-text
DN 142:255716
TI Prediction of antihypertensive efficacy of angiotensin converting enzyme inhibitors based on the β 2-adrenergic receptor (ADRB2) gene polymorphism
IN Xing, Houkun; Huang, Guo; Zhang, Yan; Peng, Shaojie; Li, Dong; Wang, Binyan; Chen, Guangliang; Huang, Aiqun; Wu, Di
PA Anhui Institute of Biomedicine, Peop. Rep. China
SO Faming Zhuanli Shengqing Gongkai Shuomingshu, 20 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CMT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1465712	A	20040107	CN 2002-123875	20020705
CN 1781554	A	20060607	CN 2005-10115552	20020705
PRAI CN 2002-123875	A3	20020705		

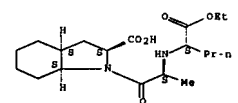
AB The test kit for evaluating the pharmacodynamic effect of angiotensin converting enzyme inhibitor (ACEI) type antihypertensives based on anal. of the polymorphism loci of β 2-adrenergic receptor (ADRB2) gene consists of primer pair, endonuclease NcoI, endonuclease buffer 4, PCR buffer, thermostable DNA polymerase Taq, and dNTPs. The PCR buffer is composed of KCl, MgCl₂, and tri(hydroxymethyl)aminomethane HCl (Tris-HCl). The endonuclease buffer 4 is composed of Tris-acetate, Mg(OAc)₂, KOAc, and DTT. The method comprises extracting genomic DNA from host cell, PCR amplifying ADRB2 gene, digesting with endonuclease, detecting the genotype of Arg16Gly locus of ADRB2 gene by electrophoresis. The order of the blood pressure-lowering rate is homozygous mutation heterozygous mutation homozygous wild type. The method for designing the software for predicting the pharmacodynamic effect of ACEI type antihypertensives is presented. The medical composition is composed of ACEI type antihypertensive and β 2-adrenergic receptor agonist or antagonist. The ACEI type antihypertensive is captopril, enalapril, cilazapril, benazepril, perindopril, ramipril, fosinopril, lisinopril, losartan, and/or valsartan. The β 2-adrenergic receptor agonist is salbutamol, terbutaline, procaterol, formoterol, clorphenaline, and/or salmeterol. The β 2-adrenergic receptor antagonist is propranolol, labetalol, nadolol, and/or celiprolol.

IT 82834-16-8, Perindopril
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(prediction of antihypertensive efficacy of angiotensin converting enzyme inhibitors based on β 2-adrenergic receptor (ADRB2) gene

functional substance. The comps. provide improved bioavailability and improved delivery of the drug into the cutaneous tissues. For example, methotrexate complex with L-lysine was found to have less skin irritation when applying topically to treat psoriasis on the forearm.

IT 82834-16-0P, Perindopril, complexes with amino acid deriva.
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USBS (Uses)
(topical comps. containing acidic active ingredient complexes with amino acids and their derivs. for improved skin care and treatment of skin conditions)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

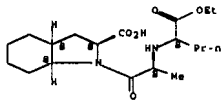


L8 ANSWER 109 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
AN 2004-740158 CAPLUS Full-text
DN 141:243893
TI Process for preparation of perindopril and its salts
IN Datta, Debashish; Singh, Girij Pal; Godbole, Himanshu Madhav; Siyan, Rajinder Singh
PA Lupin Limited, India
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CMT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004075889	A1	20040910	WO 2003-IN42	20030328
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RN:	BW, GH, GM, KE, LS, MW, MZ, SD, SE, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GW, GM, ML, MR, NE, NG, TD, TG			
CA 2517205	A1	20040910	CA 2003-2517205	20030228
AU 2003224420	A1	20040917	AU 2003-224420	20030228
EP 1603558	A1	20051214	EP 2003-720846	20030228
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			

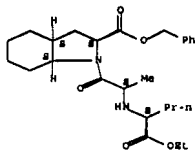
10576386 221 of 361
JP 2006519168 T 20060824 JP 2004-568714 20030228
US 2006276659 A1 20061207 US 2006-547243 20060621
PRAI WO 2003-11442 W 20030228
CA 2888822 141:243833; MARPAT 141:243833
AB A process for the preparation of perindopril and its salts involves reaction of N-[(1S)-1-(ethoxycarbonyl)butyl]-L-alanyl chloride (I) or bromide with (2S)-indolinecarboxylic acid benzyl ester or its hexahydro derivative, followed by catalytic hydrogenation. Thus, perindopril benzyl ester was prepared by adding a slurry of 1.88 g I (preparation given) to a solution of 1.6 g (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester and triethylamine in CH₂Cl₂ at -10 to 15° over 25-30 min. Hydrogenation of the benzyl ester over 10% Pd-C afforded 1.3 g perindopril.
IT a284-16-0, Perindopril
RL IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 122454-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (Preparation of perindopril and its salts)
RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

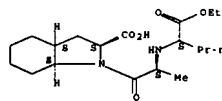
Absolute stereochemistry.



10576386 223 of 361
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
✓ ANSWER 111 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM
AN 2004:490720 CAPLUS Full-text
DN 141:59698
TI ACE inhibitors having antioxidant and NO-donor activity and use for cardiovascular, renal and diabetes-associated disorders
IN Haj-Yehia, Abdullah Ibrahim; Khan, Mohamed Amin; Qadri, Bashir Ali
PA Yissum Research Development Company of the Hebrew University of Jerusalem, Israel
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2004/050084 A2 20040617 WO 2003-111006 20031127
WO 2004/050084 A3 20040930
W: AR, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VC, VM, VU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, ME, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GQ, GW, ML, MR, NE, NG, TD, TG
AU 2003286389 A1 20040623 AU 2003-286389 20031127
EP 1578413 A2 20050928 EP 2003-777134 20031127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 2006166894 A1 20060127 US 2005-536628 20051219
PRAI US 2002-429864P P 20021129
US 2002-430003P P 20021129
WO 2003-111006 W 20031127
QB MARPAT 141:59698
AB The present invention provides multifunctional ACE inhibitor compds. that combine ACE-inhibiting activity with capability to scavenge superoxide and other reactive oxygen species, and that may further function as nitric oxide (NO) donors. The compds. are useful for preventing or treating various disorders, including cardiovascular, renal and diabetes-associated disorders. This invention is further directed to a method for treating and preventing a disorder in which treatment with an ACE inhibitor is indicated, and mainly cardiovascular disorders, renal disorders, and diabetes-associated disorders. The use of said compds. in the preparation of a medicament is further provided.
IT a284-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ACE inhibitors having antioxidant and NO-donor activity and use for cardiovascular, renal and diabetes-associated disorders)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

10576386 222 of 361
RE.CNT THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
✓ ANSWER 110 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM
AN 2004:490720 CAPLUS Full-text
DN 141:23870
TI Inhibition of angiotensin I-converting enzyme induces radioprotection by preserving murine hematopoietic short-term reconstituting cells
AU Charrier, Sabine; Michaud, Annie; Badaoui, Sabrina; Giroux, Sebastien; Ekan, Eric; Sainteny, Françoise; Corvol, Pierre; Vainchenker, William
CS Institut National de la Santé et de la Recherche Médicale (INSERM), Hematopoiese et Cellules Souches, Institut Gustave Roussy, Villejuif, Fr.
SO Blood (Apr.), 104(4), 978-985
CODEN: BLOODH, 1956; 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Angiotensin I-converting enzyme (ACE) inhibitors can affect hematopoiesis by several mechanisms including inhibition of Angiotensin II formation and increasing plasma concns. of AcSDKP (acetyl-N-Ser-Asp-Lys-Pro), an ACE substrate and a neg. regulator of hematopoiesis. We tested whether ACE inhibition could decrease the hematopoietic toxicity of lethal or sublethal irradiation protocols. In all cases, short treatment with the ACE inhibitor perindopril protected against irradiation-induced death. ACE inhibition accelerated hematopoietic recovery and led to a significant increase in platelet and red cell counts. Pretreatment with perindopril increased bone marrow cellularity and the number of hematopoietic progenitors (granulocyte macrophage colony-forming unit [CFU-GM], erythroid burst-forming unit [BFU-E], and megakaryocyte colony-forming unit [CFU-MK]) from day 7 to 28 after irradiation. Perindopril also increased the number of hematopoietic stem cells with at least a short-term reconstitutive activity in animals that recovered from irradiation. To determine the mechanism of action involved, we evaluated the effects of increasing AcSDKP plasma concns. and of an angiotensin II type 1 (AT1) receptor antagonist (telmisartan) on radioprotection. We found that the AT1-receptor antagonism mediated similar radioprotection as the ACE inhibitor. These results suggest that ACE inhibitors and AT1-receptor antagonists could be used to decrease the hematopoietic toxicity of irradiation.
IT 82834-16-0, Perindopril
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ACE inhibition induces radioprotection by preserving hematopoietic short-term reconstituting cells)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



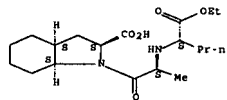
10576386 224 of 361
Absolute stereochemistry. Rotation (-).
✓ ANSWER 112 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM
AN 2004:427629 CAPLUS Full-text
DN 140:407114
TI Method for synthesis of perindopril and its pharmaceutically-acceptable salts
IN Dubuffet, Thierry; Langlois, Pascal
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI EP 1422236 A1 20040526 EP 2003-292865 20031119
EP 1422236 B1 20070214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
AT 353910 T 20070315 AT 2003-292865 20031119
ES 2282587 T3 20071016 ES 2003-3292865 20031119
WO 2005054277 A1 20050616 WO 2004-FR2937 20041118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VC, VM, VU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, ME, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GQ, GW, ML, MR, NE, NG, TD, TG
PRAI EP 2003-292865 A 20031119
QB MARPAT 140:407114
AB Perindopril was prepared by cyclization of (2S)-3-(2-bromophenyl)-2-[(1S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]propanoyl]amino]propanoic acid (I) or its esters in the presence of a Pd-based catalyst and a base (e.g., Pd(dppf)Cl₂, Pd(dppf)Cl₂, and Cs₂CO₃), followed by catalytic hydrogenation. Intermediate I was prepared by coupling of N-[(1S)-1-carboxybutyl]-L-alanine N-carboxyanhydride with (S)-2-bromophenylalanine.
IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 82834-16-0 CAPLUS

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CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 107133-36-SP, Perindopril erbumine

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation);

(synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 107133-36-8 CAPLUS

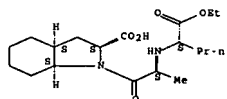
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

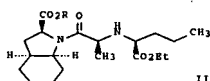
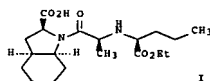
CMF C4 H11 N



10576386

227 of 361

EP 1488427 A1 20060809 EP 2006-76083 20031118
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LV, FI, RO, CY, TR, BG, CZ, EE, HU, SK
 JP 2006520320 T 20060907 JP 2004-552875 20031118
 AT 352555 T 20070215 AT 2003-775565 20031118
 CN 1966519 A 20070523 CN 2006-10166603 20031118
 ES 2279188 T3 20070816 ES 2003-3775565 20031118
 MX 2005PA05333 A 20050816 MX 2005-PA5333 20050518
 IN 2005MN00599 A 20051007 IN 2005-MN599 20050613
 US 2006063941 A1 20060323 US 2005-535187 20051031
 IN 2006MN01471 A 20070824 IN 2006-MN1471 20061204
 PRAI GB 2002-26885 A 20021118
 CN 2003-80108700 A3 20031118
 EP 2003-775565 A3 20031118
 WO 2003-GB4981 W 20031118
 IN 2005-MN599 A3 20050613
 OS CASREACT 140:407109; MARPAT 140:407109
 GI



AB Perindopril (I), or a pharmaceutically acceptable salt thereof, may be prepared from a protected ester II (R = aralkyl, CH₂Ph) via hydrogenolysis in the presence of a noble metal catalyst, such as Pd/charcoal, in the presence of a base. For example, when the base is tert-butylamine, it forms a pharmaceutically-acceptable addition salt with I, thus forming perindopril erbumine, 1-tert-butylamine salt. A monohydrate of I, or a pharmaceutically acceptable salt thereof, is also claimed and may be prepared by hydrating I, or a pharmaceutically acceptable salt thereof, by way of addition of water or by drying in air. Perindopril erbumine monohydrate was prepared and studied by x-ray diffraction. Perindopril monohydrates may be used as angiotensin converting enzyme (ACE) inhibitors.

IT 559267-97-1P, Perindopril erbumine monohydrate

RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(crystal structure; preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)

RN 690267-97-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

10576386

226 of 361

IT 695141-30-4P

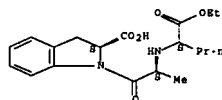
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 695141-30-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3-dihydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 113 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004.405692 CAPLUS Full-text

LA 140:407109

TI Hydrogenolysis of benzyl ester of perindopril for preparing perindopril

monohydrates for use as inhibitors of angiotensin converting enzyme (ACE)

IN Rao, Dharmaraj Ramachandra; Kankan, Rajendra Narayanrao

PA Cipla Limited, India

SO Brit. UK Pat. Appl., 16 pp.

CODEN: BAXXDU

DT Patent

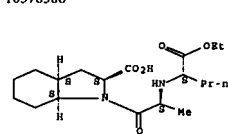
LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2395195	A	20040519	GB 2002-26885	20021118
CA 2506587	A1	20040603	CA 2003-2506587	20031118
WO 2004046172	A1	20040603	WO 2003-GB4981	20031118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RM: BW, GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, NG, TD, TG				
AU 2003283588	A1	20040615	AU 2003-283588	20031118
EP 1565485	A1	20050824	EP 2003-775565	20031118
EP 1565485	B1	20070124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015703	A	20051025	BR 2003-15703	20031118
CN 1738830	A	20060222	CN 2003-80108700	20031118

10576386

228 of 361



CM 2

CRN 75-64-9

CMF C4 H11 N



IT 82834-16-0P, Perindopril

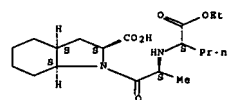
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 122454-52-8

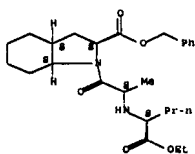
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)

RN 122454-52-8 CAPLUS

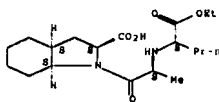
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



IT 107133-36-6P, Perindopril erbumine
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)
 RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)
 CM 1
 CRN 82834-16-0
 CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

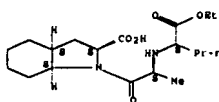


CM 2
 CRN 75-64-9
 CMP C4 H11 N



INDEX NAME)

Absolute stereochemistry. Rotation (-).



LS ANSWER 115 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2004:405663 CAPLUS Full-text

DN 140:375491
 TI Method for the synthesis of perindopril and its pharmaceutically-acceptable salts
 IN Dubuffet, Thierry; Lecouve, Jean-Pierre
 PA Les Laboratoires Servier, Fr.
 SO Eur. Pat. Appl., 6 pp.
 CODEN: EPXXDM
 DT Patent
 LA French
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1420029	A2	20040519	EP 2003-293084	20031210
EP 1420029	A3	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004131285	A1	20050721	AU 2004-312185	20041209
CA 2548405	A1	20050721	CA 2004-2548405	20041209
WO 2005066198	A1	20050721	WO 2004-FR3166	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO				
CN 1890259	A	20070103	CN 2004-80036354	20041209
BR 2004017423	A	20070308	BR 2004-17423	20041209
IN 2006DN03063	A	20070824	IN 2006-DN03063	20060529
MX 2006PA06562	A	20060731	MX 2006-PA6562	20060609
US 2007093663	A1	20070424	US 2006-582283	20060609
US 7279583	B2	20071009		
NO 2006003012	A	20060628	NO 2006-3012	20060628
PRAI EP 2003-293084	A	20031210		
WO 2004-FR3166	M	20041209		
OS CASREACT 140:375492				

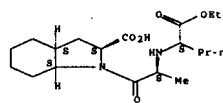
RE.CNT THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 114 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2004:405664 CAPLUS Full-text

DN 140:375492
 TI Method for synthesis of (2S,3aS,7aS)-1-[(S)-alanyl]octahydro-1H-indole-2-carboxylic acid derivatives and use in the synthesis of perindopril
 IN Dubuffet, Thierry; Lecouve, Jean-Pierre
 PA Les Laboratoires Servier, Fr.
 SO Eur. Pat. Appl., 6 pp.
 CODEN: EPXXDM
 DT Patent
 LA French
 FAN.CNT 1

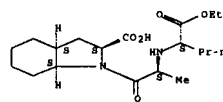
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1420030	A2	20040519	EP 2003-293085	20031210
EP 1420030	A3	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004131286	A1	20050721	AU 2004-312186	20041209
CA 2548406	A1	20050721	CA 2004-2548406	20041209
WO 2005066199	A1	20050721	WO 2004-FR3167	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO				
CN 1890259	A	20070103	CN 2004-80036942	20041209
BR 2004017540	A	20070327	BR 2004-17540	20041209
IN 2006DN03063	A	20070824	IN 2006-DN03063	20060529
MX 2006PA06563	A	20060731	MX 2006-PA6563	20060609
US 2007123581	A1	20070531	US 2006-582419	20060609
US 7288661	B2	20071030		
NO 2006003027	A	20060628		
PRAI EP 2003-293085	A	20031210		
WO 2004-FR3167	M	20041209		
OS CASREACT 140:375492; MARPAT 140:375492				
AB A method for the synthesis of the title perindopril intermediate involves coupling of (2S)-indoline-2-carboxylic acid benzyl ester or (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester or their salts with N-protected L-alanine in the presence of a coupling agent (e.g., O-(benzotriazol-1-yl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate), followed by hydrogenation over Pd.				
IT 82834-16-0P, Perindopril RL: PMU (Preparation, unclassified); PREP (Preparation) (preparation of alanyloctahydroindolecarboxylic acid deriva. in synthesis of perindopril)				
RN 82834-16-0 CAPLUS				
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)				

AB A method for the synthesis of perindopril involves coupling of (2S)-indoline-2-carboxylic acid benzyl ester or (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester with N-[(S)-1-carboxybutyl]-L-alanine in the presence of a coupling agent (e.g., O-(benzotriazol-1-yl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate), followed by hydrogenation over Pd. Perindopril was converted into its tert-butylamine salt.
 IT 82834-16-0P, Perindopril
 RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (synthesis of perindopril and its pharmaceutically-acceptable salts)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)
 Absolute stereochemistry. Rotation (-).



IT 107133-36-6P, Perindopril erbumine
 RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (synthesis of perindopril and its pharmaceutically-acceptable salts)
 RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)
 CM 1
 CRN 82834-16-0
 CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2
 CRN 75-64-9

CMP C4 H11 N



IT 122454-52-6

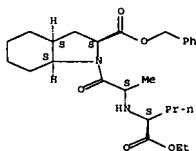
RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 116 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:405662 CAPLUS [Full-text](#)

DN 140:375490

TI Method for the synthesis of perindopril and its pharmaceutically-acceptable salts

IN Dubuffet, Thierry; Langlois, Pascal

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 8 pp.

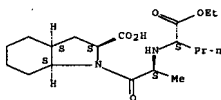
CODEN: EPXXDW

DT Patent

LA French

FAN: CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1420028	A2	20040519	EP 2003-292864	20031119
EP 1420028	A3	20040526		
EP 1420028	B1	20070221		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, ER, HU, SK				
AT 354586	T	20070315	AT 2003-292864	20031119
ES 2282586	T3	20071016	ES 2003-3292864	20031119
AU 2004295132	A1	20050616	AU 2004-295132	20041118
CA 2546506	A1	20050616	CA 2004-2546506	20041118



RN 107133-36-8 CAPLUS

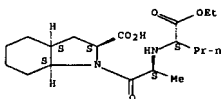
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N



IT 685141-30-4

RL: RCT (Reactant); RACT (Reactant or reagent)

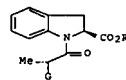
(synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 685141-30-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]-2,3-dihydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

WO 2005054276	A1	20050616	WO 2004-FR2936	20041118
W: AS, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, BG, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GQ, GW, ML, MR, ME, SN, TD, TG				
CN 1882607	A	20061220	CN 2004-80033686	20041118
BR 2004016746	A	20070116	BR 2004-16746	20041118
IN 2006DN02563	A	20070810	IN 2006-DN2563	20060508
MX 2006PA05607	A	20060817	MX 2006-PA5607	20060518
US 2007083052	A1	20070412	US 2006-580148	20060518
US 7208607	B1	20070424		
NO 2006002599	A	20060606	NO 2006-2599	20060606
PRAI EP 2003-292864	A	20031119		
WO 2004-FR2936	M	20041118		
OS CASREACT 140:375490; MARPAT 140:375490				
GI				



AB A method for the synthesis of perindopril involves reaction of indolinecarboxylate derivs. I (R = H or a protective group, G = Cl, Br, OH, TsO, MeSO₃ or CF₃SO₃) with (S)-PrCH(NH₂)CO₂Et (II), followed by catalytic hydrogenation. II was prepared by reaction of (S)-2-BrC₆H₄CH₂CH(NH₂)CO₂R with (R)-MeCH(OMe)COCl and intamol. coupling, e.g., in the presence of Pd(dba)₃, P(tolyl)₃, and Cs₂CO₃. Perindopril was converted into its tert-butylamine salt.

IT 82834-16-0P, Perindopril 107133-36-8P

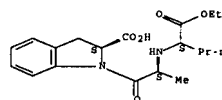
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 685141-29-1P

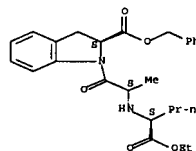
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 685141-29-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]-2,3-dihydro-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 117 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:333698 CAPLUS [Full-text](#)

DN 140:357333

TI Preparation of aroylhydroxypyrazoles for treatment of metabolic disorders

IN Semple, Graeme; Shin, Young Jun

PA Arena Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 125 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN: CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004033431	A2	20040422	WO 2003-US31509	20031002
WO 2004033431	A3	20040729		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CO, CI, CM, GA, GN, GG, GW, ML, MR, NE, SN, TD, TG

AU 2003242679 A1 20040504 AU 2003-282679 20031002

PRAI US 2002-416193P P 20021004

US 2002-417132P P 20021007

WO 2003-0831509 W 20031002

OS MARPAT 140:257333

GI

AB Title compds. [I; R1 = alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, benzyl, optionally substituted with 21 halo, OH, cyano, NO2, haloalkyl, amino, aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl, alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfinyl, alkylsulfonyl, haloalkylthio, haloalkylsulfinyl, haloalkylsulfonyl, alkylureyl, arylureyl, R2 = H, alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, phenoxy, heteroaryl, optionally substituted with 21 halo, OH, cyano, nitro, haloalkyl, amino, aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl, alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfinyl, alkylsulfonyl, haloalkylthio, haloalkylsulfinyl, haloalkylsulfonyl, alkylureyl or arylureyl groups; Ar = (substituted) pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, were prepared for the treatment of metabolic-related disorders, including dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, type 2 diabetes, Syndrome-X and the like (no data). Thus, nicotinic chloride, 2-methyl-5-propyl-2,4-dihydropyrazol-3-one, and Ca(OH)2 were heated at 90° in dioxane for 2 h, to give (5-hydroxy-1-methyl-3-propyl-1H-pyrazol-4-yl)pyridin-3-ylmethanone. I may be used in combination with other active agents such as glucosidase inhibitors, aldose reductase inhibitors, biguanides, HMG-CoA reductase inhibitors, squalene synthesis inhibitors, fibrates, LDL catabolism enhancers, angiotensin converting enzyme inhibitors, and insulin secretion enhancers.

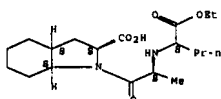
IT 2234-16-0, Perindopril

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Absolute stereochemistry. Rotation (-).



RE CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 119 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

2004:266899 CAPLUS Full-text

140:253918

TI Method for synthesis of (2S,3aS,7aS)-1-[(S)-alanyl]octahydro-1H-indole-2-carboxylic acid derivatives for use in the synthesis of perindopril

IN Dubuffet, Thierry; Langlois, Pascal

PA Les Laboratoires Servier, Fr.; Servier Lab

SO Eur. Pat. Appl., 9 pp.

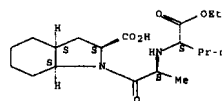
CODEN: EPXXDW

DT Patent

LA French

FAN CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1403277	A1	20040331	EP 2003-290486	20030228
EP 1403277	B1	20051005		
R1: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 305939	T	20051015	AT 2003-290486	20030228
PT 1403277	T	20051130	PT 2003-290486	20030228
ES 2246991	T3	20060401	ES 2003-3290486	20030228
AU 2004218202	A1	20040916	AU 2004-218202	20040227
WO 2004078708	A2	20040916	WO 2004-FR445	20040227
WO 2004078708	A3	20041014		
W1: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, RW, BW, GH, GM, KE, LS, LM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CO, CI, CM, GA, GN, GG, GW, ML, MR, NE, SN, TD, TG				
CN 1753907	A	20060329	CN 2004-80005406	20040227
JP 2006519176	T	20060824	JP 2006-500162	20040227
IN 2005DN03205	A	20070525	IN 2005-DN3205	20050720
US 2006149082	A1	20060706	US 2005-547132	20050824
US 7157485	B2	20070102		
PRAI EP 2003-290486	A	20030228		
WO 2004-FR445	A	20040227		



ANSWER 118 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

2004:266899 CAPLUS Full-text

140:253919

TI Process for the synthesis of N-[(S)-1-(ethoxycarbonyl)butyl]- (S)-alanine for use in the synthesis of perindopril

IN Breard, Fabienne; Lecouve, Jean-Pierre

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 9 pp.

CODEN: EPXXDW

DT Patent

LA French

FAN CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1403278	A1	20040331	EP 2003-292404	20030930
EP 1403278	B1	20050608		
R1: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 297407	T	20050615	AT 2003-292404	20030930
PT 1403278	T	20050930	PT 2003-292404	20030930
ES 2240926	T3	20051016	ES 2003-3292404	20030930
WO 2005033127	A1	20050414	WO 2004-FR2463	20040929
W1: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SR, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, LM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CO, CI, CM, GA, GN, GG, GW, ML, MR, NE, SN, TD, TG				

PRAI EP 2003-292404 A 20030930

OS MARPAT 140:253919

AB Perindopril intermediate (S)-EtO2CPr-L-Ala-OH was prepared by condensation of L-alanine alkyl or benzyl ester with Et glyoxylate or Et chloro(cyclohexyloxy)acetate, followed by allylation with allylzinc bromide, and catalytic hydrogenation.

IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PREP (Preparation)

(synthesis of [(ethoxycarbonyl)butyl]alanine for use in preparation of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

benzyl ester with N-protected alanine, followed by catalytic hydrogenation. I benzyl ester was prepared by reaction of 1-(1-cyclohexen-1-yl)pyrrolidine with (R)-1-CH2CH(NBoc)CO2CH2Ph (Boc = tert-butoxycarbonyl), followed by deprotection and cyclization.

IT 82834-16-0P, Perindopril

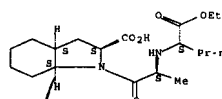
RL: PNU (Preparation, unclassified); PREP (Preparation)

(synthesis of alanyl octahydroindolecarboxylic acid derivs. for synthesis of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 120 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

2004:266897 CAPLUS Full-text

140:253917

TI Process for the synthesis of perindopril and its pharmaceutically-acceptable salts

IN Dubuffet, Thierry; Langlois, Pascal

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 9 pp.

CODEN: EPXXDW

DT Patent

LA French

FAN CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1403275	A1	20040331	EP 2003-290485	20030228
EP 1403275	B1	20051019		
R1: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 307139	T	20051115	AT 2003-290485	20030228
ES 2250846	T3	20060416	ES 2003-3290485	20030228
AU 2004217599	A1	20040916	AU 2004-217599	20040227
WO 2004078107	A2	20040916	WO 2004-FR446	20040227
WO 2004078107	A3	20041021		
W1: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, RW, BW, GH, GM, KE, LS, LM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CO, CI, CM, GA, GN, GG, GW, ML, MR, NE, SN, TD, TG				

GO, GW, ML, MR, NE, SN, TD, TG

CN 1753906 A 20060329 CN 2004-80005405 20040227
 JP 2006519177 T 20060824 JP 2006-500163 20040227
 IN 2005DN03206 A 20070525 IN 2005-DN3206 20050720
 US 2006149081 A1 20060706 US 2005-547131 20050824
 US 7166633 B2 20070123
 HK 1086281 A1 20071005 HK 2006-106195 20060529
 PRAI EP 2003-290485 A 20030228
 WO 2004-FR446 A 20040227

OS MARPAT 140:253917

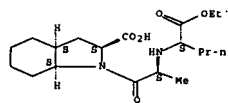
AB A method for the synthesis of perindopril involves coupling of (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid (I) or an ester with N-[(S)-1-carboxybutyl]-L-alanine, followed by catalytic hydrogenation. I benzyl ester tosylate was prepared by reaction of 1-(1-cyclohexen-1-yl)pyrrolidine with (R)-1CH₂CH(NBoc)CO₂CH₂Ph (Boc = tert-butoxycarbonyl), followed by deprotection and cyclization. Perindopril was converted into its tert-butylamine salt.

IT 82834-16-0F, Perindopril 107133-36-9P
 RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



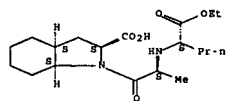
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



PI EP 1400531 A1 20040324 EP 2003-292405 20030930
 EP 1400531 B1 20060104

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

AT 315046 T 20060215 AT 2003-292405 20030930
 ES 225693 T3 20060716 ES 2003-3292405 20030930
 WO 2005031128 A1 20050414 WO 2004-FR2464 20040929

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RM: BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2003-292405 A 20030930

OS MARPAT 140:253916

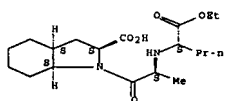
AB (S)-EtO₂CCHPr-L-Ala-OH was prepared by a multistep procedure starting with allylation of Et glyoxylate with allylzinc bromide. Subsequent steps were resolution using Pseudomonas fluorescens lipase, triflation of (R)-EtO₂CCH(OH)CH₂CH₂, substitution reaction with L-alanine, and catalytic hydrogenolysis.

IT 82834-16-0F, Perindopril
 RL: PNU (Preparation, unclassified); PREP (Preparation)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 122 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2004:203796 CAPLUS Full-text
 DN 140:253571

TI Preparation of N-phenyl or N-heterocyclic dibenzylamine compounds as inhibitors of cholesterol ester transfer protein (CETP) and medicinal use thereof

IN Maeda, Kimiya; Nagamori, Hironobu; Nakamura, Hiroshi; Shinkai, Hideo; Suzuki, Yasunori; Takahashi, Daisuke; Taniguchi, Toshio

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 121 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 2004:247009 CAPLUS Full-text
 DN 140:253916

TI Process for the synthesis of N-[(S)-1-(ethoxycarbonyl)butyl]- (S)-alanine for use in preparation of perindopril

IN Brard, Fabienne; Lecouve, Jean-Pierre
 PA Les Laboratoires Servier, Fr.
 SO Eur. Pat. Appl., 9 pp.
 CODEN: EPXDXM

DT Patent
 LA French

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PA Japan Tobacco Inc., Japan
 SO PCT Int. Appl., 207 pp.
 CODEN: PIXXD2

DT Patent
 LA Japanese

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2004020393 A1 20040311 WO 2003-JP11041 20030829

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RM: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2464846 A1 20040311 CA 2003-246486 20030829

AU 2003261826 A1 20040319 AU 2003-261826 20030829

BR 2003006208 A 20041013 BR 2003-6208 20030829

JP 2004323504 A 20041118 JP 2003-308156 20030829

JP 3630676 B2 20050316

CN 1617850 A 20050518 CN 2003-802383 20030829

EP 1533292 A1 20050525 EP 2003-791414 20030829

EP 1533292 B1 20070214

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

TR 200401413 T1 20050621 TR 2004-1413 20030829

NZ 532494 A 20060331 NZ 2003-532494 20030829

RU 2293078 C2 20070210 RU 2004-119546 20030829

AT 353870 T 20070315 AT 2003-791414 20030829

ES 2277142 T3 20070701 ES 2003-791414 20030829

EP 1829858 A2 20070905 EP 2007-3011 20030829

EP 1829858 A3 20071003

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR, AL, LT, LV, MK

ZA 2004001137 A 20050425 ZA 2004-1137 20040423

IN 2004CN0889 A 20060113 IN 2004-CN889 20040428

MX 2004PA05350 A 20040927 MX 2004-PA5350 20040603

NO 2004002584 A 20040618 NO 2004-2584 20040618

US 2005059810 A1 20050317 US 2004-503185 20041012

HK 1077567 A1 20070914 HK 2005-109494 20051026

PRAI JP 2002-255604 A 20020830

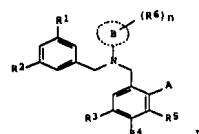
JP 2003-107161 A 20030410

EP 2003-791414 A3 20030829

WO 2003-JP11041 W 20030829

OS MARPAT 140:253571

GI



AB Dibenzylamine compds. represented by the general formula (I) (R1, R2 = halo, NO2, cyano, C1-6 alkyl, halo-C1-6 alkyl; R3, R4, R5 = H, halo, each optionally halo-substituted C1-6 alkyl, C1-6 alkylthio, or C1-6 alkoxy; or R3 and R4 or R4 and R5 together with the carbon atoms bonded thereto form an (un)substituted halo- or heterocyclic ring; A = NR7R8; wherein R7, R8 = H, each (un)substituted C1-6 alkyl or C4-10 cycloalkyl, etc.; the ring B = aryl or heterocyclyl; R6 = H, halo, NO2, NH2, HO, cyano, acyl, C1-6 alkoxy, (un)substituted C2-6 alkenyl; n = an integer of 1-3) or prodrugs thereof or pharmaceutically acceptable salts thereof are prepared. These compds. have selective and potent CETP inhibitory activity, which results in lowering intermediate-d. lipoprotein (IDL), very low d. lipoprotein (VLDL), and low d. lipoprotein (LDL) which promote arteriosclerosis, and increasing high d. lipoprotein (HDL), and are hence usable as, e.g., therapeutic or preventive drugs for hyperlipemia and arteriosclerosis. Thus, 17 mg NaH was added to a solution of 132 mg N-[3-(N-cyclopentylmethyl-N-ethylamino)-5,6,7,8-tetrahydronaphthalen-2-ylmethyl]-(2-methyl-2H-tetrazol-5-yl)amine in 2 mL DMF, followed by adding 114 mg 3-bromomethyl-5-trifluoromethylbenzonitrile, and the resulting mixture was stirred at room temperature overnight to give, after workup and silica gel chromatog., 44% 3-[[N-[3-(N-cyclopentylmethyl-N-ethylamino)-5,6,7,8-tetrahydronaphthalen-2-ylmethyl]-N-(2-methyl-2H-tetrazol-5-yl)amino]methyl]-5-trifluoromethylbenzonitrile (II). II in vitro inhibited the activity of CETP in whole blood plasma with IC50 of 0.08 μM.

IT 107133-36-8, Perindopril erbumine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antihypertensive, combination therapy; preparation of N-PH or N-heterocyclidibenzylamine compds. as inhibitors of cholesteryl ester transfer protein (CETP) for treatment or prevention of hyperlipemia and arteriosclerosis)

RN 107133-36-8 CAPLUS

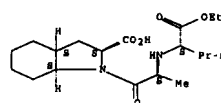
CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N



RE.CNT 10

THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 123 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

2004:145230 CAPLUS Full-text

DN 141:219619

TI Rationale and design of a large-scale trial using nicorandil as an adjunct to percutaneous coronary intervention for ST-segment elevation acute myocardial infarction: Japan-working groups of acute myocardial infarction for the reduction of necrotic damage by a K-ATP channel opener (J-WIND-KATP)

AU Minamino, Tetsuo; Kim, Jiyoung; Asakura, Masanori; Shintani, Yasunori; Asanuma, Hiroshi; Kitakaze, Masafumi

CS J-WIND Investigators, Japan Foundation for Aging and Health for Medical Frontier Strategy Research by Health and Labor Sciences Research Grants, National Cardiovascular Center, Suita, Japan

SO Circulation Journal (2004), 68(2), 101-106

CODEN: CJIOBY, ISSN: 1346-9843

PB Japanese Circulation Society

DT Journal

LA English

AB Background: The benefits of percutaneous coronary intervention (PCI) in acute myocardial infarction (AMI) are limited by reperfusion injury. In animal models, nicorandil, a hybrid of an ATP-sensitive K⁺ (KATP) channel opener and nitrates, reduces infarct size, so the Japan-Working groups of acute myocardial infarction for the reduction of Necrotic Damage by a K-ATP channel opener (J-WIND-KATP) designed a prospective, randomized, multicenter study to evaluate whether nicorandil reduces myocardial infarct size and improves regional wall motion when used as an adjunctive therapy for AMI. Methods and Results: Twenty-six hospitals in Japan are participating in the J-WIND-KATP study. Patients with AMI who are candidates for PCI are randomly allocated to receive either i.v. nicorandil or placebo. The primary end-points are (1) estimated infarct size and (2) left ventricular function. Single nucleotide

(4-lymophosphatase (SNPs) that may be associated with the function of KATP-channel and the susceptibility of AMI to the drug will be examined Furthermore, a data mining method will be used to design the optimal combined therapy for post-myocardial infarction (MI) patients. Conclusions: It is intended that J-WIND-KATP will provide important data on the effects of nicorandil as an adjunct to PCI for AMI and that the SNPs information that will open the field of tailor-made therapy. The optimal therapeutic drug combination will also be determined for post-MI patients.

IT 107133-36-8, Perindopril erbumine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nicorandil and cardiovascular agent for decreasing risk of cardiac events in patients with post-myocardial infarction)

RN 107133-36-8 CAPLUS

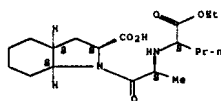
CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 124 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

2004:145229 CAPLUS Full-text

DN 141:219275

TI Rationale and design of a large-scale trial using atrial natriuretic peptide (ANP) as an adjunct to percutaneous coronary intervention for

ST-segment elevation acute myocardial infarction: Japan-working groups of acute myocardial infarction for the reduction of necrotic damage by ANP (J-WIND-ANP)

AU Asakura, Masanori; Kim, Jiyoung; Minamino, Tetsuo; Shintani, Yasunori; Asanuma, Hiroshi; Kitakaze, Masafumi

CS J-WIND Investigators, Japan Society for the Promotion of Science for Young Scientists, Osaka University Graduate School of Medicine, Suita, Japan

SO Circulation Journal (2004), 68(2), 95-100

CODEN: CJIOBY, ISSN: 1346-9843

PB Japanese Circulation Society

DT Journal

LA English

AB Background: The benefits of percutaneous coronary intervention (PCI) in acute myocardial infarction (AMI) are limited by reperfusion injury. In animal models, atrial natriuretic peptide (ANP) reduces infarct size, so the Japan-Working groups of acute myocardial infarction for the reduction of Necrotic Damage by ANP (J-WIND-ANP) designed a prospective, randomized, multicenter study, to evaluate whether ANP as an adjunctive therapy for AMI reduces myocardial infarct size and improves regional wall motion. Methods and Results: Twenty hospitals in Japan will participate in the J-WIND-ANP study. Patients with AMI who are candidates for PCI are randomly allocated to receive either i.v. ANP or placebo administration. The primary end-points are (1) estimated infarct size (E-creatinine kinase and troponin T) and (2) left ventricular function (left ventriculograms). Single nucleotide polymorphisms (SNPs) that may be associated with the function of ANP and susceptibility of AMI will be examined Furthermore, a data mining method will be used to design the optimal combinational therapy for post-MI patients. Conclusions: J-WIND-ANP will provide important data on the effects of ANP as an adjunct to PCI for AMI and the SNPs information will open the field of tailor-made therapy. The optimal therapeutic drug combination will also be determined for post-MI patients.

IT 107133-36-8, Perindopril erbumine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug therapy for data mining of cardiovascular therapy combination; large-scale trial rationale and design using atrial natriuretic peptide (ANP) as adjunct to PCI for ST-segment elevation acute myocardial infarction patients)

RN 107133-36-8 CAPLUS

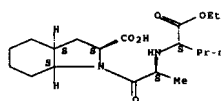
CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMP C4 H11 N

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 125 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
2004:36709 CAPLUS Full-text

DN 140:59939

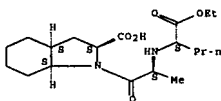
TI Method for synthesis of perindopril and its pharmaceutically acceptable salts

IN Dubuffet, Thierry; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.; Servier Lab
SO Eur. Pat. Appl., 7 pp.
CODEN: EPXXDM

DT Patent
LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1380591	A1	20040114	EP 2003-292132	20030829
EP 1380591	B1	20051116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 310012	T	20051215	AT 2003-292132	20030829
ES 2252633	T3	20060516	ES 2003-3292132	20030829
AU 2004270428	A1	20050317	AU 2004-270428	20040827
WO 2005023842	A1	20050317	WO 2004-FR2197	20040827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1835966	A	20060920	CN 2004-80023535	20040827
JP 2007526902	T	20070930	JP 2006-524395	20040827
IN 2006DN00922	A	20070810	IN 2006-DN922	20060222
US 2007010572	A1	20070111	US 2006-569537	20060223
PRAI EP 2003-292132	A	20030829		
WO 2004-FR2197	W	20040827		
OS CASREACT 140:59939; MARPAT 140:59939				



CM 2

CRN 75-64-9
CMP C4 H11 N

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 126 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
2004:36708 CAPLUS Full-text

DN 140:59938

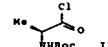
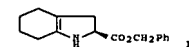
TI Method for synthesis of perindopril and its pharmaceutically acceptable salts

IN Dubuffet, Thierry; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDM

DT Patent
LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1380590	A1	20040114	EP 2003-292131	20030829
EP 1380590	B1	20060906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 338766	T	20060915	AT 2003-292131	20030829
ES 2272922	T3	20070501	ES 2003-3292131	20030829
AU 2004270427	A1	20050317	AU 2004-270427	20040827
WO 2005023841	A1	20050317	WO 2004-FR2196	20040827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				



AB A method for the synthesis of perindopril and its tert-Bu amine salt is described. The steps are: coupling of hexahydroindolecarboxylate I with propionyl chloride II in CH2Cl2, followed by Boc deprotection with TPA and reaction with Et 2-oxopentanoate and hydrogenation over Pd/C. Addition of tert-butylamine to perindopril provides the salt.

IT 52834-16-0P, Perindopril 107133-36-8P

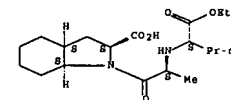
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of perindopril and tert-butylamine salt)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CN 1839147	A	20060927	CN 2004-80024192	20040827
JP 2007526901	T	20070920	JP 2006-524394	20040827
IN 2006DN00918	A	20070810	IN 2006-DN918	20060222
US 2007043103	A1	20070222	US 2006-570566	20060227
US 7183308	B1	20070227		
PRAI EP 2003-292131	A	20030829		
WO 2004-FR2196	W	20040827		

OS CASREACT 140:59938; MARPAT 140:59938

AB A method for the synthesis of perindopril and its pharmaceutically acceptable salts involves coupling of (2S)-2,3,4,5,6,7-hexahydro-1H-indolecarboxylic acid or its benzyl ester with R2-L-Ala-X (R2 is a protective group, X is halo), followed by deprotection, reaction with (R)-PrCH(G)CO2Et (G is Cl, Br, I, or tosyloxy), and catalytic hydrogenation. Addition of tert-butylamine to perindopril provides the salt.

IT 52834-16-0P, Perindopril 107133-36-8P

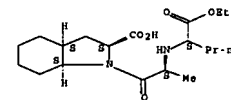
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of perindopril and tert-butylamine salt)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

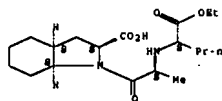
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMP C4 H11 N

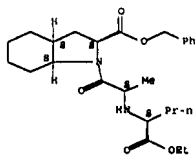
IT 122454-52-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of perindopril and tert-butylamine salt)

RN 122454-52-8 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LAW NUMBER 127 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM

AN 2003:985781 CAPLUS [Full-text](#)

DN 140:28049

TI Method for synthesis of perindopril and its pharmaceutically acceptable

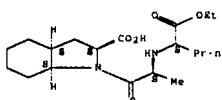
IT 122454-16-0P 122454-52-8P

RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of perindopril and its tert-Bu amine salt)

RN 122454-16-0 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

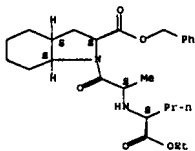
Absolute stereochemistry. Rotation (-).



RN 122454-52-8 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



IT 107133-36-9P

RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of perindopril and its tert-Bu amine salt)

RN 107133-36-8 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 122454-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

salts [2003/26]

IN Dubuffet, Thierry; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.; Servier Lab
SO Eur. Pat. Appl., 8 pp.

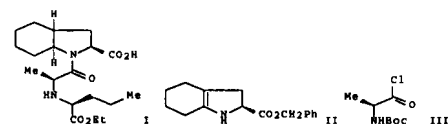
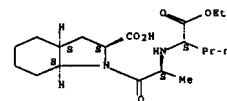
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1371659	A1	20031217	EP 2003-292133	20030829
EP 1371659	B1	20051012		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
AT 306496	T	20051015	AT 2003-292133	20030829
ES 2250853	T3	20060416	ES 2003-3292133	20030829
AU 2004270429	A1	20050317	AU 2004-270429	20040827
AU 2004270429	B2	20070524		
WO 2005023843	A1	20050317	WO 2004-FR2198	20040827
M:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, HT, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CN 1835965	A	20060920	CN 2004-80023532	20040827
IN 2006DN00919	A	20070810	IN 2006-DN919	20060222
US 2007088168	A1	20070419	US 2006-570565	20060227
US 722387	B2	20070529		
PRAI EP 2003-292133	A	20030829		
WO 2004-FR2198	N	20040827		
OS CASREACT 140:28049; MARPAT 140:28049				
GI				

AB A method for the synthesis of perindopril (I) and its tert-Bu amine salt is described. The steps are: coupling of (hexahydro)indolecarboxylate II with propionyl chloride III in CH₂Cl₂, followed by Boc deprotection with TFA, reaction with Et 2-oxopentanoate under reductive conditions, and removal of benzyl ester by hydrogenation to give I. Addition of tert-Bu amine to I provides the salt.

CM 2

CRN 75-64-9
CMP C4 H11 NRE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LAW NUMBER 128 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM

AN 2003:947713 CAPLUS [Full-text](#)

DN 139:381760

TI Method for synthesis of perindopril and its pharmaceutically acceptable

IN Dubuffet, Thierry; Lecouve, Jean-Pierre

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 8 pp.

CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1367061	A1	20031203	EP 2003-291601	20030630
EP 1367061	B1	20060104		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
AT 315043	T	20060215	AT 2003-291601	20030630
ES 2256689	T3	20060716	ES 2003-3291601	20030630
AU 2004253721	A1	20050113	AU 2004-253721	20040628
WO 2005003153	A1	20050113	WO 2004-FR1637	20040628
M:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, HT, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,			

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CN 1802384 A 20060712 CN 2004-80016014 20040628
IN 2005DN05718 A 20070427 IN 2005-DN5718 20051209
US 2006178421 A1 20060810 US 2005-562490 20051222
US 7179833 B2 20070220

PRAI EP 2003-291601 A 20030630
WO 2004-FR1637 W 20040628

OS CASREACT 139:381760; MARPAT 139:381760

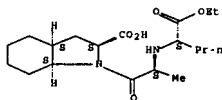
AB A method for the synthesis of perindopril and its pharmaceutically acceptable salts (e.g., the tert-butylamine) involves cyclocondensation reaction of N-[(S)-1-carboxybutyl]-[(S)-alanine with sulfinyl chlorides R1SOCl (R1 = imidazolyl, benzimidazolyl, or tetrazolyl) to give Et (2S)-2-[(4S)-4-methyl-2,5-dioxo-1,2,3-oxathiazolidin-3-yl]pentanoate, which is amidated with (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid and hydrogenated over 10% Pt/C to give perindopril.

IT 82834-16-0F, Perindopril 107133-36-0F
122454-52-8F
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril via cyclocondensation of carboxybutylalanine with imidazolesulfinyl chloride)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

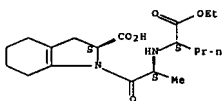
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



RE.CN 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 129 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
2003:910218 CAPLUS Full-text
139:365227

TI New process for the synthesis of N-[(S)-1-carboxybutyl]-[(S)-alanine esters and their use in the synthesis of perindopril

IN Breard, Fabienne; Fugler, Claude

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 5 pp.

CODEN: EPXXDW

DT Patent

LA French

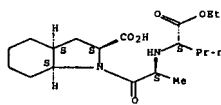
FAN.CMT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1362845	A2	20031119	EP 2003-292145	20030901
EP 1362845	A3	20040331		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004270432	A1	20050317	AU 2004-270432	20040831
CA 2536926	A1	20050317	CA 2004-2536926	20040831
WO 2005023755	A1	20050317	WO 2004-FR2213	20040831
M: AR, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MO, MU, MV, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SV, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: BM, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

CN 1815911 A 20060920 CN 2004-80023534 20040831
BR 2004011901 A 20061024 BR 2004-13901 20040831
JP 2007504203 T 20070301 JP 2006-525159 20040831
US 2006252958 A1 20061109 US 2006-569472 20060222
MX 2006PA02229 A 20060517 MX 2005-PA2229 20060227
NO 2006001152 A 20060310 NO 2006-1152 20060310
PRAI EP 2003-292145 A 20030901
WO 2004-FR2213 W 20040831

OS CASREACT 139:365227; MARPAT 139:365227

AB Title: alanine derivs. (S)-R02CHPr-L-Ala-OH (R = C1-C6 alkyl) were prepared from N-protected (S)-5-methyl-2-morpholinone by propylation or allylation/hydrogenation, ring opening by LiOH, esterification, oxidation of



CM 2

CRN 75-64-9

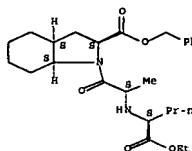
CMF C4 H11 N



RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



IT 625095-50-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril via cyclocondensation of carboxybutylalanine with imidazolesulfinyl chloride)

RN 625095-50-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)- (SCI) (CA INDEX NAME)

Absolute stereochemistry.

the hydroxy group, and deprotection. In an example, N-[(S)-1-carboxybutyl]-[(S)-alanine hydrochloride was prepared via allylation of Boc-protected (S)-5-methyl-2-morpholinone and treatment of tert-Bu (3S,5S)-5-methyl-3-propyl-2-oxo-4-morpholinecarboxylate with LiOH in aqueous MeCN and then EtI to afford intermediate Et (2S)-2-[(tert-butoxycarbonyl)amino]-2-hydroxy-1-methylethyl]amino]pentanoate.

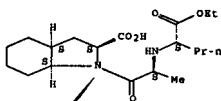
IT 82834-16-0F, Perindopril

RL: FNU (Preparation, unclassified); PREP (Preparation)
(process for synthesis of N-[(S)-carboxybutyl]-L-alanine esters for use in synthesis of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



ANSWER 130 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
2003:909172 CAPLUS Full-text
139:396166

TI Method for synthesis of perindopril and its pharmaceutically acceptable salts

IN Dubuffet, Thierry; Lecouve, Jean-Pierre

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 8 pp.

CODEN: EPXXDW

DT Patent

LA French

FAN.CMT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1362864	A1	20031119	EP 2003-291600	20030630
EP 1362864	B1	20070425		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 360638 T 20070515 AT 2003-291600 20030630				
AU 2004255899 A1 20050120 AU 2004-255899 20040628				
WO 2005005461 A2 20050120 WO 2004-FR1638 20040628				
WO 2005005461 A3 20050331				
M: AR, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SV, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RM: BM, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG

CN 1805972 A 20060719 CN 2004-80016324 20040628
IN 2005085717 A 20070427 IN 2005-085717 20051209
US 200614884 A 20060706 US 2005-562950 20051223
US 7220776 B2 20070522

PRA1 EP 2003-291600 A 20030630
WO 2004-PR1628 W 20040628

OS CABSREACT 139:396166; MARPAT 139:396166

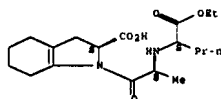
AB Perindopril and its pharmaceutically acceptable salts (e.g., tert-butylamine salt) are prepared by the cyclocondensation reaction of N-[(8)-carboethoxy-1-butyl]-2-(2S)-2-[(4S)-4-methyl-2,5-dioxo-1,3-oxazolidin-3-yl]pentanone which is amidated with (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid in the presence of an acid (e.g., hydrochloric acid) to give (2S)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid which is hydrogenated with a 10% Pt/C catalyst to give perindopril which is then salted with tert-butylamine to give perindopril tert-butylammonium salt.

IT 625095-50-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate, in a method for synthesis of perindopril and its pharmaceutically acceptable salts)

RN 625095-50-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

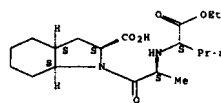


IT 625095-50-3P, Perindopril
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate, in a method for synthesis of perindopril and its pharmaceutically acceptable salts)

RN 625095-50-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 107133-36-8P
RL: SPN (Synthetic preparation); PREP (Preparation) (method for synthesis of perindopril and its pharmaceutically acceptable salts)

RN 107133-36-8 CAPLUS

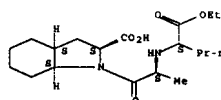
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 131 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM
2003:875244 CAPLUS Full-text
139:364424

TI Method of preparing amine stereoisomers via reduction of sulfinylamines in presence of chiral auxiliaries

IN Han, Zhengxu; Krishnamurthy, Dhileepkumar; Senanayake, Chris Hugh; Lu, Zhi-hui

PA Apsintem, Llc., USA

SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2

DT Patent

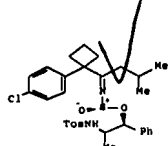
LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003091207	A2	20031106	WO 2003-US8827	20030407
WO 2003091207	A3	20040916		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, ME, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VC, VN, YU, ZA, ZM, ZW			
RW:	OH, OM, KE, LS, MM, ME, SD, SE, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KE, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, NR, SN, TD, TG			
CA 2482432	A1	20031106	CA 2003-2482432	20030407
AU 2003253588	A1	20031110	AU 2003-253588	20030407
EP 1497272	A2	20050119	EP 2003-747253	20030407
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2005522525	T	20050728	JP 2003-587772	20030407
CN 1659154	A	20050824	CN 2003-813204	20030407
IN 20040802806	A	20050401	IN 2004-DN2806	20040921
MX 2004PA09843	A	20050816	MX 2004-PA9843	20041008
US 2005165240	A1	20050728	US 2005-508944	20050302
US 7129378	B2	20041031		
US 2006247539	A1	20061221	US 2006-514141	20060901
PRA1 US 2003-271158P	P	20030410		
WO 2003-US8827	W	20030407		
US 2005-508943	A1	20050302		

OS MARPAT 139:364424

GI



AB A method of preparing amine stereoisomers comprises stereoselectively reducing a sulfinylamine or sulfinylamine stereoisomer that bears on the sulfinyl group a residue of an alkyl, thiol or amine with a source of a nucleophile to afford

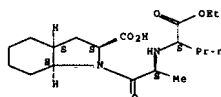
a sulfinylamine stereoisomer, followed by contacting the sulfinylamine stereoisomer with a reagent suitable for the cleavage of a sulfur-nitrogen bond, to afford an amine stereoisomer. The intermediates may also be used in the preparation of sulfoxide and sulfinylamine stereoisomers. Thus, 1-(4-chlorophenyl)cyclobutanecarbonitrile was treated with Me2CHCH2MgCl and (2S,4R,5S)-4-methyl-5-phenyl-3-tosyl-1,2,3-oxathiazolidine 2-oxide to give the intermediate imine I which was reduced with NaBH4 in presence of Ti(OEt)4 to give (R)- diisemethylalbutramine, isolated as its D-tartrate.

IT 82834-16-0P, Perindopril
RL: SPN (Synthetic preparation); PREP (Preparation) (method of preparing amine stereoisomers via reduction of sulfinylamines in presence of chiral auxiliaries)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



ANSWER 132 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM
2003:832153 CAPLUS Full-text
139:308016

TI Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril

IN Dubuffet, Thierry; Langlois, Pascal

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1354876	A1	20031022	EP 2003-291420	20030613
EP 1354876	B1	20050427		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
AT 294161	T	20050515	AT 2003-291420	20030613
PT 1354876	T	20050630	PT 2003-291420	20030613
ES 2240921	T3	20051016	ES 2003-3291420	20030613
WO 2005003093	A1	20050113	WO 2004-FR1427	20040609
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SV, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VC, VN, YU, ZA, ZM, ZW			

RW: BM, CH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2003-291420 A 20030613

OS MARPAT 139:308016

AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its alkyl esters, intermediates used in the synthesis of perindopril, were prepared by condensation of 2-(hydroxymethyl)cyclohexanone with glycine benzyl or alkyl ester to give (2S,3aS)-3,4,4',5,6,7-hexahydro-2H-indole-2-carboxylic acid esters, which underwent catalytic hydrogenation of the double bond and resolution using a chiral amine. In an example, (2S,3aS,7aS)-perhydroindole-2-carboxylic acid was prepared with chemical purity 98% and enantiomeric purity 99%.

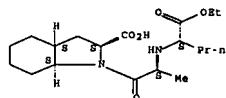
IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PRSP (Preparation) (method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as perindopril intermediates)

RN 82834-16-0 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 133 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2003:832152 CAPLUS [Full-text](#)

DN 139:308015

TI Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril

IN Dubuffet, Thierry; Lecouve, Jean-Pierre

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1354875	A1	20031022	EP 2003-291157	20030519
EP 1354875	B1	20041124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 283258	T	20041215	AT 2003-291157	20030519

PT 1354875 T 20050331 PT 2003-291157 20030519

ES 2233914 T3 20050616 ES 2003-3291157 20030519

WO 2004101969 A1 20041202 WO 2004-FR1225 20040519

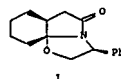
R: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BM, CH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2003-291157 A 20030519

OS CASREACT 139:308015; MARPAT 139:308015

GI



AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its alkyl or benzyl esters, intermediates used in the synthesis of perindopril, were prepared by condensation of 2-oxocyclohexylacetic acid with (S)-phenylglycinol to give lactam I, reductive ring opening of the oxazole ring, cleavage of the 2-hydroxy-1-phenylethyl group, reaction with triflic anhydride, cyanation, hydrolysis of the cyano group, and hydrogenation of the double bond. In an example, (2S,3aS,7aS)-perhydroindole-2-carboxylic acid was obtained as the tosylate in enantiomeric purity 99%.

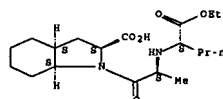
IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PRSP (Preparation) (method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as perindopril intermediates)

RN 82834-16-0 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 134 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2003:832151 CAPLUS [Full-text](#)

DN 139:308014

TI Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril

IN Dubuffet, Thierry; Langlois, Pascal

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 11 pp.

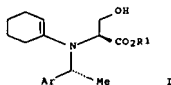
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1354874	A1	20031022	EP 2003-290931	20030415
EP 1354874	B1	20041124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 283257	T	20041215	AT 2003-290931	20030415
PT 1354874	T	20050331	PT 2003-290931	20030415
ES 2233913	T3	20050616	ES 2003-3290931	20030415
WO 2004092133	A1	20041028	WO 2004-FR858	20040407
R: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BM, CH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG				
PRAI EP 2003-290931 A 20030415				
OS CASREACT 139:308014; MARPAT 139:308014				
GI				



AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its alkyl or benzyl esters, intermediates used in the synthesis of perindopril, were prepared by

condensation of L-serine alkyl or benzyl ester with acetophenone deriv. ArCOME (Ar = alkylphenyl or naphthyl), reduction of the imine formed, reaction with cyclohexanone to give I, halohydroxylation, radical cyclization, and deprotection. In an example, (2S,3aS,7aS)-perhydroindole-2-carboxylic acid was obtained with chemical purity 98% and enantiomeric purity 99%.

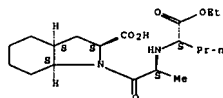
IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PRSP (Preparation) (method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as perindopril intermediates)

RN 82834-16-0 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 135 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2003:832150 CAPLUS [Full-text](#)

DN 139:307680

TI Preparation of the L-arginine salt of perindopril and its use as an ACE inhibitor

IN Damien, Gerard; Lefoulon, Francois; Marchand, Bernard

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 5 pp.

CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1354873	A1	20031022	EP 2003-290383	20030217
EP 1354873	B1	20040714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
FR 2838648	A1	20031024	FR 2002-4647	20020418
FR 2838648	B1	20040521		
WO 2003087050	A2	20031023	WO 2003-FR507	20030217
WO 2003087050	A3	20040325		
R: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KE, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003222921 A1 20031027 AU 2003-222921 20030217
 AT 271036 T 20040715 AT 2003-290383 20030217
 PT 1354873 T 20041029 PT 2003-290383 20030217
 ES 2224092 T3 20050301 ES 2003-3290383 20030217
 ZA 2003001395 A 20030902 ZA 2003-1395 20030220
 US 2003199568 A1 20031023 US 2003-371865 20030221
 US 6696481 B2 20040224
 NO 2003000849 A 20031020 NO 2003-849 20030224
 AU 2003200700 A1 20031106 AU 2003-200700 20030227
 NZ 524478 A 20040528 NZ 2003-524478 20030228
 CN 1481656 A 20031029 CN 2003-107148 20030307
 MK 2003PA03346 A 20050926 MK 2003-PA03346 20030318
 BR 2003000709 A 20040908 BR 2003-709 20030321
 JP 2003321493 A 20031111 JP 2003-83250 20030325
 JP 3737488 B2 20060118
 CA 2423825 A1 20031018 CA 2003-2423825 20030403
 CA 2423825 C 20060221
 HK 1087367 A1 20051014 HK 2004-100189 20040110
 PR 2002-4847 A 20020418
 WO 2003-FR8507 W 20030217

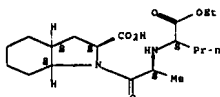
AB The L-arginine salt of perindopril, which has increased storage stability over the corresponding butylamine salt, is prepared, and its use for the treatment of hypertension and cardiac insufficiency is claimed.

IT 22034-16-0, Perindopril
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of the L-arginine salt of perindopril and its use as an ACE inhibitor)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 612548-45-5P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of the L-arginine salt of perindopril and its use as an ACE inhibitor)

RN 612548-45-5 CAPLUS

CN L-Arginine, (2S,3aS,7aS)-1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:1) (CA INDEX NAME)

CN 1

KG, KE, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003218213 A1 20031008 AU 2003-218213 20030314
 US 2005232925 A1 20051020 US 2005-508317 20050616
 PRAI US 2002-365165P P 20020318
 WO 2003-U88121 W 20030314

AB The present invention features pharmaceutical compns. and methods to inhibit angiogenesis, with implications to cancer therapy. These methods are based on the discovery that activated thrombin has antiangiogenic activity and that this antiangiogenic activity is at least in part, mediated through the activation of a class of thrombin receptors termed, protease-activated receptor (PAR). Pharmaceutical compns. and methods are also directed to a class of proteases which mediate this activation, particularly the urokinase plasminogen activator (uPA) polypeptide.

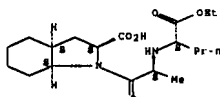
IT 82834-16-0, Perindopril

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (ACE inhibitor; PAR receptor-mediated antiangiogenic activity of thrombin and use of PAR receptor agonists for treatment of cancer and other angiogenesis-associated diseases)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



AB NUMBER 137 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2003:771360 CAPLUS Full-text

DN 139:277168

TI Method for the synthesis of (2S)-indoline-2-carboxylic acid for use in the synthesis of perindopril

IN Souvira, Jean-Claude; Lecouve, Jean-Pierre

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 6 pp.

CODEN: EPXXDW

DT Patent

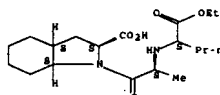
LA French

PAN: CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1348684	A1	20031001	EP 2003-290879	20030409
EP 1348684	B1	20060308		
AT 319668	T	20060315	AT 2003-290879	20030409
PT 1348684	T	20060531	PT 2003-290879	20030409

CRN 82834-16-0
 CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

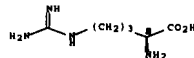


CN 2

CRN 74-79-3

CMP C6 H14 N4 O2

Absolute stereochemistry.



RE: CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB NUMBER 136 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2003:777526 CAPLUS Full-text

DN 139:286322

TI PAR receptor-mediated antiangiogenic activity of thrombin and use of PAR receptor agonists for the treatment of cancer and other angiogenesis-associated diseases

IN Sukhrie, Vikas P.; Merchant, Jaime; Chan, Barden

PA Beth Israel Deaconess Medical Center, USA

SO PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DT Patent

LA English

PAN: CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003079978	A2	20031002	WO 2003-US8121	20030314
WO 2003079978	A3	20040226		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	OH, OM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY,			

ES 2260585 T3 20061101 ES 2003-3290879 20030409
 AU 2004230294 A1 20041028 AU 2004-230294 20040407
 CA 2521877 A1 20041028 CA 2004-2521877 20040407
 WO 2004092095 A1 20041028 WO 2004-FR857 20040407

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SJ, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, OM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

BR 2004009095 A 20060411 BR 2004-9095 20040407
 CN 1768019 A 20060503 CN 2004-80009239 20040407
 JP 2006522034 T 20060928 JP 2006-500155 20040407
 IN 2005DM04126 A 20070831 IN 2005-DM04126 20050913
 US 2006183919 A1 20060817 US 2005-552676 20051007
 US 7196204 B2 20070327
 NO 2005005257 A 20051109 NO 2005-5257 20051109
 US 2007112204 A1 20070517 US 2007-649980 20070105
 PRAI EP 2003-290879 A 20030409
 WO 2004-FR857 W 20040407
 US 2005-552676 A3 20051007

AB (2S)-indoline-2-carboxylic acid, an intermediate used in the synthesis of perindopril, was prepared by resolution of racemic indoline-2-carboxylic acid by reaction with (R)-α-methylbenzylamine. In an example, (2S)-indoline-2-carboxylic acid was obtained with enantiomeric purity > 99.5 %.

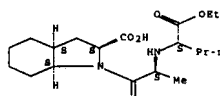
IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PREP (Preparation)
 (synthesis of (2S)-indoline-2-carboxylic acid via resolution as intermediate in synthesis of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE: CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB NUMBER 138 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2003:738076 CAPLUS Full-text

DN 139:250328

TI Compressed tablets based on microcapsules having modified release

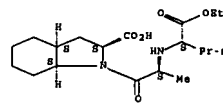
IN Jorda, Rafael; Autant, Pierre
 PA Flamel Technologies, Fr.
 SO Fr. Demande, 46 pp.
 CODEN: FRXXBL
 DT Patent
 LA French
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 2837100	A1	20030919	FR 2002-3336	20020318
CA 2479057	B1	20040723	CA 2003-2479057	20030314
WO 2003077888	A1	20030925	WO 2003-FR827	20030314
WO 2003077888	A3	20040415		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GH, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003242818	A1	20030929	AU 2003-242818	20030314
EP 1485071	A2	20041215	EP 2003-744400	20030314
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008487	A	20050118	BR 2003-8487	20030314
CN 1642530	A	20050720	CN 2003-806302	20030314
JP 2005527522	T	20050915	JP 2003-575941	20030314
IN 2004KN01250	A	20060905	IN 2004-KN1250	20040827
MX 2004PA09010	A	20041126	MX 2004-PA9010	20040915
ZA 2004008412	A	20060830	ZA 2004-8412	20041018
US 2005266078	A1	20051201	US 2005-507886	20050623
PRAI FR 2002-3336	A	20020318		
WO 2003-FR827	W	20030314		

AB Preparation of a prolonged-release compressed tablet comprising a core containing the active principle and a coating which controls the release of active principle is disclosed. Prolonged-release microcapsules containing metformin hydrochloride crystal were prepared. A compressed tablet containing above microcapsules 769.23, mannitol 492.31, Crospovidone 230.77, aspartame 19.23, flavor 16.23, and magnesium stearate 7.69 mg.

IT 82834-16-0, Perindopril
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (compressed tablets based on microcapsules having modified release)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 139 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 2003:696857 CAPLUS Full-text
 139:230479

TI Preparation of (4-(1,1'-biphenyl-2-ylcarbonylamino or benzoylamino)phenyl)acetic acid esters as microsomal triglyceride transfer protein (MTP) inhibitors

IN Hagihara, Atsushi; Oe, Yasuhiro; Odani, Naoya; Matanabe, Shizue; Ikenogami, Taku; Kawai, Takashi; Madono, Kenya; Taniguchi, Toshio
 PA Japan Tobacco Inc., Japan
 SO PCT Int. Appl., 561 pp.
 CODEN: PIXXD2

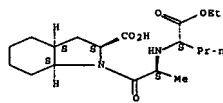
DT Patent
 LA Japanese
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003072532	A1	20030904	WO 2003-JP2398	20030228
W: AE, AG, AL, AM, AU, AZ, BA, BB, BR, BY, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GE, GR, ID, IL, IN, IS, JP, KE, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, RU, SC, SG, TJ, TM, TN, TT, UA, UG, UZ, VC, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GH, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2460682	A1	20030904	CA 2003-2460682	20030228
AU 2003211617	A1	20030909	AU 2003-211617	20030228
JP 2003321424	A	20031111	JP 2003-53869	20030228
JP 1662566	B2	20050622		
BR 2003006292	A	20040824	BR 2003-6292	20030228
EP 1479666	A1	20041124	EP 2003-743078	20030228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1630629	A	20050622	CN 2003-804734	20030228
ZA 2005002495	A	20050920	ZA 2005-2495	20030228
ZA 2005002496	A	20051012	ZA 2005-2496	20030228
NZ 531890	A	20060224	NZ 2003-531890	20030228
TU 2293721	C2	20070220	TU 2004-124370	20030228
CN 1943786	A	20070411	CN 2006-10099709	20030228
NZ 543229	A	20070531	NZ 2003-543229	20030228
MX 2004PA02602	A	20040811	MX 2004-PA2602	20040319
ZA 2004002275	A	20050423	ZA 2004-2275	20040323
IN 2004KN0460	A	20060324	IN 2004-KN460	20040407
NO 2004001872	A	20040506	NO 2004-1872	20040506
US 2005075367	A1	20050407	US 2004-492811	20041008

pg. and 268 mg 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride were dissolved in 5 mL CH₂Cl₂ and stirred at room temperature for 6 h to give, after distillation of the solvent and silica gel chromatog., 725 mg 4-[(4'-trifluoromethyl-1,1'-biphenyl-2-ylcarbonyl)amino]phenylacetic acid 2,2-bis[ethylcarbamoyl]-2-phenylethyl ester (II; R = H). II (R = H) and II (R = Me) inhibited the triglyceride transport between liposomes by MTP with IC₅₀ of 0.6 and 0.39 nM, resp., and the secretion of apolipoprotein B from HepG2 cell with IC₅₀ of 0.65 and 0.46, resp. Pharmaceutical formulations, e.g., a tablet containing 2-[(2-[(4'-trifluoromethyl-1,1'-biphenyl-2-ylcarbonyl)amino]-3-(pyrrolidinocarbonyl)phenyl)acetoxy]methyl-2-phenylmalonic acid di-Et ester, were described.

IT 82834-16-0, Perindopril
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antihypertensive agent, coadministration drugs containing; preparation of (biphenylcarbonylamino or benzoylamino)phenylacetic acid esters as microsomal triglyceride transfer protein (MTP) inhibitors for treatment or prevention of diseases)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 140 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 2003:678514 CAPLUS Full-text
 139:191440

TI Methods of treating or preventing a cardiovascular condition using a cyclooxygenase-1 inhibitor

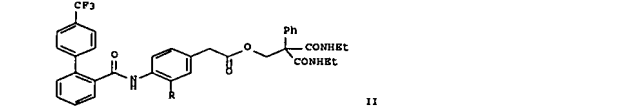
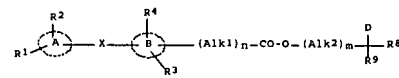
IN Kru, Elaine S.
 PA USA
 SO U.S. Pat. Appl. Publ., 32 pp.
 CODEN: USXXCO

DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003162824	A1	20030828	US 2002-292255	20021112
PRAI US 2001-331346P	P	20011112		
US 2001-338291P	P	20011113		

OS MARPAT 139:191440
 AB Methods for treating or preventing one or more cardiovascular conditions in a subject comprises treating the subject with a therapeutically effective amount

JP 2005194281	A	20050721	JP 2005-19579	20050127
JP 2005220132	A	20050818	JP 2005-19739	20050127
JP 2005220133	A	20050818	JP 2005-20179	20050127
AU 2005248950	A1	20060119	AU 2005-248950	20051223
IN 2007KN00581	A	20070706	IN 2007-KN581	20070216
PRAI JP 2002-53876	A	20020228		
AU 2003-211617	A3	20030228		
CN 2003-804734	A3	20030228		
JP 2003-53869	A3	20030228		
NZ 2003-531890	A3	20030228		
WO 2003-JP2398	W	20030228		
IN 2004-KN460	A3	20040407		
OS MARPAT 139:230479				
GI				



AB The title compds. [I; R₁, R₂ = H, C1-6 alkyl, C3-7 cycloalkyl, C1-6 alkoxy, halo-C1-6 alkyl, halo-C1-6 alkoxy, each (un)substituted C6-14 aryl, C7-16 aralkyl, C6-14 aryloxy, C7-16 aryloxy, C7-15 arylcarbonyl, heterocyclyl, or NH₂ C2-7 alkoxy, C2-6 alkenyl, the ring A = C6-14 aryl, heterocyclyl, 9-oxofluorenyl, fluorenyl; X = CO₂(CH₂)_n, each N-(un)substituted CONH(CH₂)_n or NHC(O)(CH₂)_n (wherein n = an integer of 0-3); R₃, R₄ = H, HO, halo, each (un)substituted C1-6 alkyl, heterocyclyl, or CONH₂, C1-6 alkoxy, halo-C1-6 alkyl, C7-16 aryloxy, C1-6 acyl, the ring B = phenylene, C5-7 (aza)cycloalkanediy, indollediy, benzimidazolediy, pyridinediy, pyrimidinediy, benzocycloalkanediy, quinolinediy, etc.; Alk1, Alk2 = alkanediy, alkenediy, n, m = 0-3; D = C1-6 alkyl, C2-6 alkenyl, C2-7 alkoxy, C2-7 alkoxy, NR₄2COR₄3 (wherein R₄2 = H, C1-6 alkyl, R₄3 = C4-14 aryl, C7-16 aralkyl, etc.; R₈, R₉ = H, C1-6 alkyl, (un)substituted C6-14 aryl, CONH₂, or NH₂, succinimid-2-yl, hydroxy-C1-6 alkyl, CO₂H or its ester, (CH₂)₂CO₂CH₂20 (wherein R₂₀ = H, C1-6 alkyl, C3-7 cycloalkyl; s = 0-3)] or prodrugs thereof or pharmaceutically acceptable salts of either are prepared. These compds. I selectively inhibit microsomal triglyceride transfer protein (MTP) of small intestine, are metabolized in blood or liver, and residual amount of MTP inhibitors is small enough not to substantially inhibit liver MTP and hence causes no side effects such as a fatty liver. They are useful for prevention or treatment of hyperlipidemia, arteriosclerosis, coronary artery diseases, obesity, diabetes, or hypertension. Thus, 519 mg 4-[(4'-trifluoromethyl-1,1'-biphenyl-2-ylcarbonyl)amino]phenylacetic acid (preparation given), 317 mg 2-hydroxymethyl-2-phenylmalonic acid diethylamide

of a selective cyclooxygenase-1 inhibitor or a pharmaceutically-acceptable salt, tautomer or prodrug thereof alone or in combination with either a drug used in the treatment or prevention of a cardiovascular condition or a non-drug therapy used in the treatment of a cardiovascular condition.

Cyclooxygenase-1 inhibitor: 5-(4-chlorophenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)pyrazole (I), was prepared from 4'-chloroacetophenone and (4-methoxyphenyl)hydrazine hydrochloride. I inhibited development of atherosclerosis in cholesterol-fed apoE knockout mice.

IT 4234-16-0, Perindopril

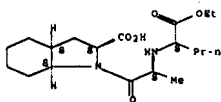
RL: BIU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(angiotensin converting enzyme inhibitor; cyclooxygenase-1 inhibitor for treating or preventing cardiovascular conditions)

RN 82834-16-0 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LE ANSWER 143 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2003:675553 CAPLUS Full-text

DN 139:197771

TI Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril

IN Dubouff, Thierry; Langlois, Pascal

PA Les Laboratoires Servier, Fr.; Servier Lab

SO Eur. Pat. Appl., 8 pp.

CODEN: EPXKXW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1338591	A1	20030827	EP 2003-290487	20030228
EP 1338591	B1	20051026		
W: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 307801	T	20051115	AT 2003-290487	20030228
ES 2250847	T3	20060416	ES 2003-3290487	20030228
AU 2004218200	A1	20040916	AU 2004-218200	20040227
WO 2004078707	A2	20040916	WO 2004-FR444	20040227
WO 2004078707	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LE ANSWER 143 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2003:670106 CAPLUS Full-text

DN 139:321745

TI The ACE Gene I/D Polymorphism Is Not Associated With the Blood

Pressure and Cardiovascular Benefits of ACE Inhibition

AU Haddad, Stephen B.; Tziroli, Christophe; Cambien, Francois; Poirier,

Odette; Raoux, Segolene; Chalmers, John; Chapman, Neil; Coleman, Samuel;

Leguennec, Solenn; MacMahon, Stephen; Neal, Bruce; Ohkubo, Takayoshi;

Woodward, Mark

CE Department of Physiology, University of Melbourne, Melbourne, Australia

SO Hypertension (2003), 42(3), 297-303

CODEN: HYPEDM; ISSN: 0194-911X

LB Lippincott Williams & Wilkins

DT Journal

LA English

AB The insertion/deletion (I/D) polymorphism of the angiotensin-converting enzyme (ACE) gene might have consequences for the risks of vascular diseases. We examined the ACE genotype and the effects of a perindopril-based blood pressure-lowering regimen on macrovascular events, dementia, and cognitive decline among hypertensive and nonhypertensive patients with a history of cerebrovascular disease. ACE I/D genotypes were measured in 5688 of 6105 individuals with previous stroke or transient ischemic attack who participated in the PROGRESS trial. The DD genotype was significantly (P<0.0001) less frequent in Asian subjects (Chinese and Japanese, 14.7%) than in non-Asian subjects (32.0%). Controlling for racial background, there were no associations between ACE genotypes and cerebrovascular disease history or cardiovascular risk factors, including baseline blood pressure. The ACE genotype was not associated with the long-term risks of stroke, cardiac events, mortality, dementia, or cognitive decline; neither did the ACE genotype predict the blood pressure reduction associated with the use of the ACE inhibitor perindopril. Similarly, there was no evidence that the ACE genotype modified the relative benefits of ACE inhibitor-based therapy over placebo. This study provides no evidence that in patients with cerebrovascular disease, knowledge of ACE genotype is useful for predicting either the risk of disease or the benefits of perindopril-based blood pressure-lowering treatment.

IT 2234-16-0, Perindopril

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ACE genotype and effects of perindopril based blood pressure lowering regimen on macrovascular events, dementia and cognitive decline among hypertensive and nonhypertensive patients with a history of cerebrovascular disease)

RN 82834-16-0 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BO, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CN 1753849 A 20060329 20040227

JP 2006519175 T 20060824 20040227

US 2006167273 A1 20060727 20050824

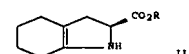
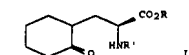
US 7157484 B2 20070102

PRAI EP 2003-290487 A 20030228

WO 2004-FR444 A 20040227

OS CASREACT 139:197771; MARPAT 139:197771

GI



AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its benzyl or alkyl esters were prepared by reaction of 1-(1-cyclohexen-1-yl)pyrrolidine with (R)-1CH2CH(NR')CO2R (R is H, benzyl, or alkyl; R' is an amine-protecting group) to afford cyclohexanone derivs. I. Cyclization of I, e.g., using p-toluenesulfonic acid, gave compds. II, which underwent catalytic hydrogenation to afford compds. of the invention. The title acid was obtained in 87% yield and 99% enantiomeric purity by this method.

IT 82834-16-0, Perindopril

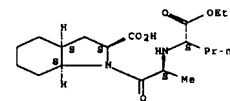
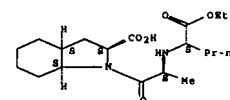
RL: PMU (Preparation, unclassified); PREP (Preparation)

(method for synthesis of perhydroindolecarboxylic acid and esters as perindopril intermediates)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LE ANSWER 143 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2003:609507 CAPLUS Full-text

DN 139:149930

TI Process for the preparation of high purity perindopril and intermediates useful in its synthesis

IN Simig, Gyula; Mezei, Tibor; Porcs-Makkay, Marta; Mandi, Attila

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 12 pp.

CODEN: EPXKXW

DT Patent

LA English

FAN.CNT 1

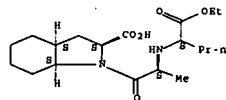
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1333026	A1	20030806	EP 2002-290206	20020130
EP 1333026	B1	20070627		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 365714	T	20070715	AT 2002-290206	20020130
IN 2003MUG0069	A	20050128	IN 2003-MUG9	20030117
CA 2474003	A1	20030807	CA 2003-2474003	20030129
WO 2003064388	A2	20030807	WO 2003-18691	20030129
WO 2003064388	A3	20040205		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZW				
RN: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 2003000231	A2	20030828	HU 2003-231	20030129
EE 200400107	A	20041015	EE 2004-107	20030129
BR 2003007293	A	20041221	BR 2003-7293	20030129
CN 1622936	A	20050601	CN 2003-802714	20030129
JP 2005521667	T	20050721	JP 2003-564011	20030129
NZ 534168	A	20061130	NZ 2003-534168	20030129
AP 1741	A	20070630	AP 2004-3091	20030129
US 2005119492	A1	20050602	US 2004-503272	20040729
MX 2004PA07444	A	20050617	MX 2004-PA7444	20040730
NO 2004003472	A	20040820	NO 2004-3472	20040820
BO 108858	A	20050531	BO 2004-108858	20040827
HK 1076101	A1	20070518	HK 2005-108134	20050916

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US 2007197821 A1 20070823 US 2007-788454 20070420
 US 7279595 B2 20071009
 PRAI EP 2002-290206 A 20020130
 WO 2003-18591 W 20030129
 US 2004-503272 A3 20040729
 OS MARPAT 139:149930
 AB The invention relates to 1-[2(S)-1-(S)-(ethoxycarbonyl)butylamino]propionyl 1-(3aS,7aS)octahydroindole-2(S)-carboxylic acid (perindopril) and its tert-butylamine salt, free of contaminants derivable from dicyclohexylcarbodiimide, and a process for their synthesis. The invention also relates to N-[1-(ethoxycarbonyl)butyl]-N-(alkoxycarbonyl)alanine intermediates used in the synthesis of perindopril, a known ACE inhibitor. Thus, N-[1-(ethoxycarbonyl)butyl]-N-(ethoxycarbonyl)alanine, prepared by ethoxycarbonylation of N-[1-(ethoxycarbonyl)butyl]alanine, was treated with thionyl chloride in CH₂Cl₂ and acylated by perhydroindole-2-carboxylic acid in THF at reflux for 4-4.5 h. The product was treated with tert-butylamine to afford 55% perindopril eburnine.
 IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril eburnine
 RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 useful (process for preparation of high purity perindopril and intermediates in its synthesis)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



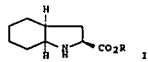
RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)
 CM 1
 CRN 82834-16-0
 CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

10576386

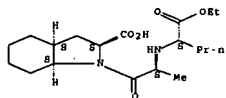
283 of 361

ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GM, ML, MR, NE, SN, TD, TG
 PRAI EP 2003-290607 A 20030312
 OS CASREACT 139:69148; MARPAT 139:69148
 GI



AB Title compds. I [R = H, CH₂Ph, alkyl] were prepared by treating 2,7-oxypanedione with XCH₂CH(NHR₂)CO₂R₁ [R₁ = CH₂Ph, alkyl; R₂ = protective group] to give HO₂C(CH₂)₄CO₂CH₂CH(NHR₂)CO₂R₁ which was cyclized to the lactam, cyclized to the indole with Ti, and reduced over Pt, Pd, Rh, or Ni catalyst. Thus, I [R = H] was prepared from 2,7-oxypanedione and (2S)-1CH₂CH(NHCO₂Me)₂CO₂CH₂Ph in 5 steps.
 IT 82834-16-0P, Perindopril
 RL: PNU (Preparation, unclassified); PREP (Preparation)
 (method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

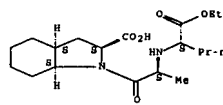


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 145 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 AN 003:488613 CAPLUS Full-text
 DN 139:22503
 TI Method for the synthesis of perindopril and its pharmaceutically-acceptable salts
 IN Dubuffet, Thierry; Lecouve, Jean-pierre
 PA Les Laboratoires Servier, Fr.
 SO Eur. Pat. Appl., 9 pp.
 CODEN: EPXKDW
 DT Patent
 LA French

10576386

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CM 2
 CRN 75-64-9
 CMP C4 H11 N



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 144 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
 DN 139:69148
 TI Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril
 IN Dubuffet, Thierry; Lecouve, Jean-pierre
 PA Les Laboratoires Servier, Fr.
 SO Eur. Pat. Appl., 11 pp.
 CODEN: EPXKDW
 DT Patent
 LA French
 PAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1323729	A1	20030702	EP 2003-290607	20030312
EP 1323729	B1	20041103		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
AT 281465	T	20041115	AT 2003-290607	20030312
PT 1323729	T	20050228	PT 2003-290607	20030312
ES 2231760	T3	20050516	ES 2003-3290607	20030312
WO 2004083237	A1	20040930	WO 2004-FR592	20040312
M:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SV, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	BW, GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GM, ML, MR, NE, SN, TD, TG			

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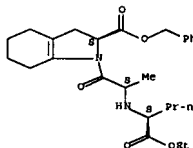
PAN.CNT 1
 PATENT NO. KIND DATE APPLICATION NO. DATE
 PI EP 1321471 A1 20030625 EP 2003-290605 20030312
 EP 1321471 B1 20050504
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 AT 294814 T 20050515 AT 2003-290605 20030312
 PT 1321471 T 20050729 PT 2003-290605 20030312
 ES 2240919 T3 20051016 ES 2003-3290605 20030312
 WO 2004083238 A1 20040930 WO 2004-FR594 20040312
 M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SV, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RM: BW, GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GM, ML, MR, NE, SN, TD, TG

PRAI EP 2003-290605 A 20030312
 OS CASREACT 139:22503; MARPAT 139:22503
 AB Perindopril and its pharmaceutically-acceptable salts were prepared from 2,7-oxypanedione by a multistep procedure, i.e., reaction with (R)-XCH₂CH(NHBoc)CO₂CH₂Ph (X is Br or Iodo, Boc is tert-butoxycarbonyl), cyclization of deprotected 2-amino-4-oxononanedioic acid derivative, Ti-catalyzed coupling to form the indole ring system, reaction with N-[(S)-1-carbethoxybutyl]-(S)-alanine, and catalytic hydrogenation. In an example, perindopril was obtained with enantiomeric purity 99%.

IT 539820-43-4P
 RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (method for synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 539820-43-4 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

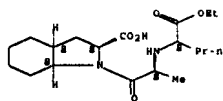
Absolute stereochemistry.



IT 82834-16-0P, Perindopril 107133-36-8P
 RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP

Preparation of (method for synthesis of perindopril and its pharmaceutically acceptable salts)
 RN 82834-16-0 CAPLUS
 CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

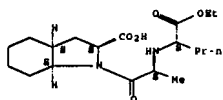
CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



protecting group; R4 is benzyl or alkyl). cyclization of deprotected 2-amino-4-oxononanedioic acid derivative, Ti-catalyzed coupling to form the indole ring system, reaction with an alanine deriv., and catalytic hydrogenation. In an example, 1 (R1 = H, R2 = tert-butoxycarbonyl) was obtained with enantiomeric purity 99%.

IT 6034-16-0P, Perindopril

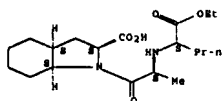
RL: PNU (Preparation, unclassified); PREP (Preparation)

(synthesis of alanyloctahydroindolecarboxylic acid deriva. for use in synthesis of perindopril)

RN 82834-16-0 CAPLUS

CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LA NUMBER 143 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2003:77804 CAPLUS Full-text

DI 138:107004

TI A process for the preparation of perindopril, its analogs and salts using 2,5-dioxoxazolidine intermediate compounds

IN Cid, Pau

PA Adir, Pr.

SO Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1279665	A2	20030129	EP 2002-16262	20020723
EP 1279665	A3	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
IN 2002MU00639	A	20040417	IN 2002-MU639	20020712
MO 2003010142	A2	20030206	MO 2002-EP8223	20020723
MO 2003010142	A3	20030828		
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MO, MK, MN, MM, MX, MY, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RM: GH, GN, KE, LS, MM, MZ, SD, SL, SZ, TG, UG, ZM, ZW, AM, AZ, BY, KO, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,				

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

LA NUMBER 146 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM

AN 2003:470308 CAPLUS Full-text

DI 139:22502

TI Method for the synthesis of (2S,3aS,7aS)-1-[(S)-alanyloctahydro-1H-indole-2-carboxylic acid derivatives for use in the synthesis of perindopril

IN Dubuffet, Thierry; Lecouve, Jean-Pierre

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 10 pp.

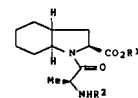
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1319668	A1	20030618	EP 2003-290606	20030312
EP 1319668	B1	20041027		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 280775	T	20041115	AT 2003-290606	20030312
PT 1319668	T	20050228	PT 2003-290606	20030312
ES 2231759	T3	20050516	ES 2003-3290606	20030312
NO 2004082357	A2	20040930	NO 2004-FRS93	20040312
NO 2004082357	A3	20041028		
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RM: BW, GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TG, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, ML, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI EP 2003-290606	A	20030312		
OS CASREACT 139:22502; MARPAT 139:22502				
GI				



AB Alanyloctahydroindolecarboxylic acid deriva. 1 (R1 is H, alkyl, or benzyl; R2 is a protecting group) were prepared from 2,7-oxepanediene by a multistep procedure, i.e., reaction with (R)-XCH2CH(MHR)CO2R4 (X is Br or Iodo; R3 is a

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AU 2002328954	A1	20030217	AU 2002-328954	20020723
AU 2002328954	B2	20071004		
HU 200202414	A2	20030228	HU 2002-2414	20020723
BR 2002011422	A	20040817	BR 2002-11422	20020723
CN 1529694	A	20040915	CN 2002-814322	20020723
JP 200501829	T	20050120	JP 2002-515501	20020723
NZ 530578	A	20070223	NZ 2002-530578	20020723
ZA 2004000323	A	20050117	ZA 2004-323	20040115
MX 2004PA00649	A	20041027	MX 2004-PA649	20040121
US 2004248814	A1	20041209	US 2004-484572	20040712
IN 2005MU00042	A	20070824	IN 2005-MU42	20050114
PRAI EP 2001-500197	A	20010724		
MO 2002-EP8223	M	20020723		
MARPAT 138:107004				

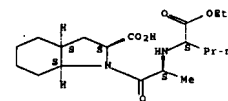
AB Perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propanoyl]octahydro-1H-indole-2-carboxylic acid) or its analogs or salts were prepared by treating RCH(CO2R4)HCH2CO2H (R4, R5 = C1-4 alkyl, R6 = C1-6 alkyl) with X2C:O (X is a leaving group) to give a 2,5-dioxoxazolidine, which reacts with octahydro-1H-indole-2-carboxylic acid or ester to give the desired product. In an example, N,N'-carbonyldiimidazole was added to a suspension of N-[(S)-1-carboxybutyl]-[S]-alanine in CH2Cl2 and the mixture kept at 0° for 1 h. (2S,3aS,7aS)-octahydroindole-2-carboxylic acid was added at -5°C and the solution kept at this temperature for 1 h to give 80% perindopril (isolated as the tert-butylamine salt).

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril
 erbumine
 RL: IMP (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
 (process for preparation of perindopril using dioxoxazolidine intermediate)

RN 82834-16-0 CAPLUS

CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS

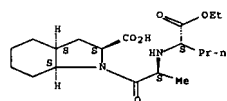
CM 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

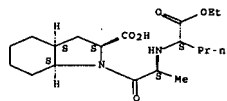


CM 2

CRN 75-64-9
CMF C4 H11 N

ANSWER 148 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
2002:866690 CAPLUS Full-text
137:353117
TI Method for synthesis of (2S,3aS,7aS)-1-(S)-alanyloctahydro-1H-indole-2-carboxylic acid derivatives as intermediates for synthesis of perindopril
IN Mezei, Tibor; Porcs-Makkay, Marta; Simig, Gyula
PA Les Laboratoires Servier S.A., Fr.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1256590	A1	20021113	EP 2002-291853	20020723
EP 1256590	B1	20060301		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
FR 2827860	A1	20030131	FR 2001-9839	20010724
FR 2827860	B1	20041210		
IN 2002MU00629	A	20040417	IN 2002-MU629	20020711
CA 2455706	A1	20030227	CA 2002-2455706	20020723
WO 2003016336	A1	20030227	WO 2002-FR2627	20020723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				



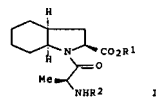
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 149 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
2002:754955 CAPLUS Full-text
137:268473
TI Porous drug matrices and methods of manufacture thereof
IN Straub, Julius; Altreuter, David; Bernstein, Howard; Chickering, Donald E.; Khattak, Sarfaraz; Randall, Greg
PA Acusphere Inc., USA
SO U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U. S. 6,395,300.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002142050	A1	20021003	US 2002-53929	20020122
US 6395300	B1	20020528	US 1999-433486	19991104
EP 1642572	A1	20060405	EP 2005-27194	20060525
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
CN 1823737	A	20060830	CN 2005-10136940	20060525
US 6645528	B1	20031111	US 2000-694407	20001023
US 6932983	B1	20050823	US 2000-706045	20001103
ZA 2001010347	A	20030730	ZA 2001-10347	20011218
US 2005048116	A1	20050303	US 2004-924642	20040824
US 2005058710	A1	20050317	US 2004-928886	20040827
FR 1999-136323P	P	19990527		
US 1999-158659P	P	19991008		
US 1999-433486	A2	19991104		
US 2000-186310P	P	20000302		
CN 2000-808161	A3	20000525		
EP 2000-939365	A3	20000525		
US 2002-53929	A3	20020122		

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrices preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solution and hydrophilic or hydrophobic excipients that stabilize the drug and inhibit crystallization, and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. Hydrophobic or hydrophilic excipients may be selected to stabilize the drug in crystalline form by inhibiting crystal growth or to stabilize the drug in amorphous form by preventing crystallization. The pore forming agent can be either a volatile

RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2002334027 A1 20030303 AU 2002-334027 20020723
BR 200201334 A 20040928 BR 2002-11334 20020723
CN 1533396 A 20040929 CN 2002-814609 20020723
JP 200500386 T 20050106 JP 2003-521258 20020723
JP 3868957 B2 20070117
NZ 530427 A 20050826 NZ 2002-530427 20020723
AT 318838 T 20060315 AT 2002-291853 20020723
PT 1256590 T 20060630 PT 2002-291853 20020723
ES 2259071 T3 20060916 ES 2002-2291853 20020723
HU 200202437 A2 20030228 HU 2002-2437 20020724
ZA 2004000246 A 20060726 ZA 2004-246 20040113
MX 2004PA00443 A 20040318 MX 2004-PA443 20040115
US 2004198988 A1 20041007 US 2004-484022 20040115
US 7060842 B2 20060613
PRAI FR 2001-9839 A 20010724
WO 2002-FR2627 W 20020723
OS CASREACT 137:353117
GI



AB Alanyloctahydroindolecarboxylic acid deriva. I (R1 = H, alkyl, benzyl, R2 is a protecting group) were prepared as intermediates for the synthesis of perindopril. Thus, treatment of Me (2S)-2,3-dihydro-1H-indole-2-carboxylate with Boc-L-Ala-OH (Boc = tert-butoxycarbonyl) in THF in the presence of Et3N and DCC for 6 h at room temperature afforded alk Me (2S)-1-[(2S)-2-[(tert-butoxycarbonyl)amino]propionyl]-2,3-dihydro-1H-indole-2-carboxylate, which was hydrogenated over Pd/C at 60°C to give 98% I (R1 = Me, R2 = Boc).

IT 82834-16-CP, Perindopril
RL: PNU (Preparation, unclassified); PEP (Preparation) (synthesis of alanyloctahydroindolecarboxylic acid deriva. as intermediates for synthesis of perindopril)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

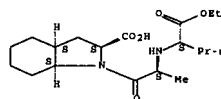
Absolute stereochemistry. Rotation (-).

liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Thus, 5.46 g of PEG 8000, 0.545 g of prednisone, and 0.055 g of Span 40 were dissolved in 182 mL of methylene chloride. A solution of 3.27 g of ammonium bicarbonate in 18.2 mL of water was added to the organic solution (phase ratio 1:10) and homogenized for 5 min at 16,000 RPM. The resulting emulsion was spray dried on a benchtop spray dryer using an air-atomizing nozzle and nitrogen as the drying gas.

IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (porous drug matrixes and methods of manufacture thereof)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

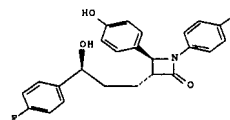


ANSWER 150 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
2002:574955 CAPLUS Full-text
137:129303
TI Combinations of azetidinone sterol absorption inhibitor(s) with cardiovascular agent(s) for the treatment of vascular conditions
IN Kossakov, Teddy; Ress, Rudyard Joseph; Strony, John; Veltri, Enrico P.; Hauer, William
PA Schering Corporation, USA
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 12

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002058731	A2	20020801	WO 2002-US1196	20020125
WO 2002058731	A3	20031120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MY, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,				

10576386		293 of 361	
		OR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, ON, GO, GW, ML, MR, NE, SN, TD, TG	
CA 2434436	A1	20020801	CA 2002-2434436 20020125
CA 2562982	A1	20020801	CA 2002-2562982 20020125
CA 2563051	A1	20020801	CA 2002-2563051 20020125
AU 2002241903	A1	20020808	AU 2002-241903 20020125
US 2003069221	A1	20030410	US 2003-07339 20020125
EP 1385545	A2	20040204	EP 2002-707500 20020125
EP 1385548	B1	20070523	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR 2002006644	A	20040225	BR 2002-6644 20020125
HU 2003003923	A2	20040301	HU 2003-3923 20020125
EP 1413331	A2	20040428	EP 2004-161 20020125
EP 1413331	A3	20040630	
EP 1413331	B1	20071003	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004517919	T	20040617	JP 2002-559065 20020125
CN 1582168	A	20050216	CN 2002-804219 20020125
EP 1541176	A2	20050615	EP 2005-3029 20020125
EP 1541176	A3	20060412	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
EP 1671650	A1	20060621	EP 2006-5831 20020125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
CN 1915429	A	20070221	CN 2006-10126233 20020125
EP 1785144	A2	20070516	EP 2007-3151 20020125
EP 1785144	A3	20070523	
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI			
AT 362757	T	20070615	AT 2002-707500 20020125
EP 1810693	A2	20070725	EP 2007-9475 20020125
EP 1810693	A3	20071017	
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI			
NZ 545332	A	20070928	NZ 2002-545332 20020125
ZA 2003005692	A	20041025	ZA 2003-5692 20030723
ZA 2003005694	A	20041025	ZA 2003-5694 20030723
ZA 2003005693	A	20050209	ZA 2003-5693 20030723
IN 2003CN01150	A	20050422	IN 2003-CN1150 20030724
NO 2003003358	A	20030912	NO 2003-3358 20030725
MX 2003PA06724	A	20031024	MX 2003-PA6724 20030725
US 2004097482	A1	20040920	US 2003-639900 20030813
HK 1060854	A1	20070907	HK 2004-103917 20040601
US 2005193982	A1	20050714	US 2004-998400 20041129
US 2006199793	A1	20060907	US 2005-158429 20050622
IN 2006CN01141	A	20070831	IN 2006-CN1141 20060403
AU 2007201970	A1	20070524	AU 2007-201970 20070503
JP 2007211031	A	20070823	JP 2007-141163 20070528
PRAI US 2001-264275P	P	20010126	
US 2001-264396P	P	20010126	
US 2001-264600P	P	20010126	
US 2001-323849P	P	20010921	
US 2001-323839P	P	20010921	
US 2001-324123P	P	20010921	
CA 2002-2434682	A3	20020125	
CN 2002-807208	A3	20020125	
EP 2002-704233	A3	20020125	

10576386		294 of 361	
EP 2002-705933	A3	20020125	
EP 2002-707500	A3	20020125	
EP 2002-707556	A3	20020125	
EP 2002-714773	A3	20020125	
JP 2002-559066	A3	20020125	
US 2002-57323	A3	20020125	
US 2002-57646	A1	20020125	
WO 2002-081196	W	20020125	
US 2002-136968	A3	20020501	
IN 2003-CN1150	A3	20030724	
AU 2006-202618	A3	20060620	
OS	MARPAT 137:129903		
GI			

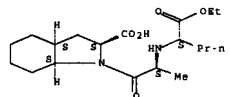


AB The present invention provides compns., therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor and (b) at least one cardiovascular agent different from the sterol absorption inhibitor, which can be useful for treating vascular conditions, obesity, diabetes and lowering plasma levels of sterols. Tablets were prepared containing cardiovascular agents which can be coadministered with formulations containing, e.g., I. The preparation of I was given.

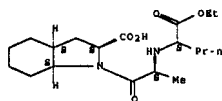
IT 82834-16-0, Perindopril 107133-36-8, Perindopril
 ER: THU (Therapeutic use), BIOL (Biological study), USES (Uses)
 (combinations of azeididone sterol absorption inhibitor(s) with cardiovascular agent(s) for the treatment of vascular conditions)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-((2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



10576386		295 of 361	
RN 107133-36-0	CAPLUS		
CN 1H-Indole-2-carboxylic acid, 1-((2S)-2-[[[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)			
CM 1			
CRN 82834-16-0			
CMP C19 H32 N2 O5			
Absolute stereochemistry. Rotation (-).			



CM 2	
CRN 75-64-9	
CMP C4 H11 N	



LA ANSWER 151 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN	
AM 2001:851113 CAPLUS Full-text	
DN 135:371632	
TI Preparation of the ACE-inhibiting β-crystalline form of perindopril tert-butylamine salt and antihypertensive pharmaceutical formulation containing it	
IN Pfeiffer, Bruno; Ginet, Yves-Michel; Coquerel, Gerard; Beilles, Stephane	
PA Adir et Compagnie, Fr.	
80 PCT Int. Appl., 14 pp.	
CODEN: PIXXD2	
DT Patent	
LA French	
PAN. CNT 1	
PATENT NO. KIND DATE APPLICATION NO. DATE	
PI WO 2001087836 A1 20011122 WO 2001-FR2168 20010706	
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,	

10576386		296 of 361	
		LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW	
RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
FR 2811319	A1	20020111	FR 2000-8792 20000706
FR 2811319	B1	20020822	
HU 2001002813	A2	20020328	HU 2001-2813 20010705
HU 2001002813	A3	20031229	
CA 2415442	A1	20011122	CA 2001-2415442 20010706
EP 1294689	A1	20030326	EP 2001-954059 20010706
EP 1294689	B1	20060426	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR 2001012244	A	20030624	BR 2001-12244 20010706
JP 2003533508	T	20031111	JP 2001-584233 20010706
JP 3592257	B2	20041124	
EE 200300002	A	20040816	EE 2003-2 20010706
NZ 523234	A	20050128	NZ 2001-523234 20010706
AP 1407	A	20050530	AP 2002-2710 20010706
AT 324367	T	20060515	AT 2001-954059 20010706
EP 1676839	A2	20060705	EP 2006-75789 20010706
EP 1676839	A3	20061108	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PT 1294689	T	20060731	PT 2001-954059 20010706
ES 2262666	T3	20061201	ES 2001-1954059 20010706
IN 2002MU00594	A	20040417	IN 2002-MU594 20020703
MX 2002PA12921	A	20040730	MX 2002-PA12921 20021219
IN 2002MN01845	A	20050204	IN 2002-MN1845 20021219
US 2004029813	A1	20040212	US 2002-312902 20021231
ZA 2003000024	A	20040205	ZA 2003-24 20030102
NO 2003000050	A	20030106	NO 2003-50 20030106
NO 323446	B1	20070507	
BG 107533	A	20031128	BG 2003-107533 20030205
HR 2003000079	A1	20030430	HR 2003-79 20030206
JP 2005002121	A	20050106	JP 2004-206159 20040713
US 20050203165	A1	20050915	US 2005-52489 20050204
US 7259181	B2	20070821	
IN 2005MU00265	A	20070330	IN 2005-MU265 20050310
SG 125974	A1	20061030	SG 2005-1529 20050311
IN 2005MN00575	A	20051007	IN 2005-MN575 20050607
AU 2006235841	A1	20061123	AU 2006-235841 20061103
FR 2000-8792	A	20000706	
AU 2001-276419	A3	20010706	
EP 2001-954059	A3	20010706	
JP 2001-584233	A3	20010706	
WO 2001-FR2168	W	20010706	
IN 2002-MU594	A3	20020703	
IN 2002-MN1845	A3	20021219	
US 2002-312902	B1	20021231	

AB The more-stable β-crystalline form of the tert-butylamine salt of perindopril (I), characterized by its X-ray powder diffraction pattern, is prepared by refluxing the tert-butylamine salt of perindopril in dichloromethane, followed by cooling the mixture, and filtration. A 1-contg tablet formulation is presented.

IT 107133-36-3
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(preparation of the ACE-inhibiting β -crystalline form of perindopril tert-butylamine salt and antihypertensive pharmaceutical formulation containing it)

RN 107133-36-8 CAPLUS

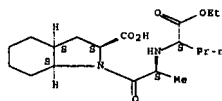
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

LA ANSWER 152 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

IN 2001:851112 CAPLUS [Full-text](#)

DN 135:371631

TI Preparation and X-ray characterization of the ACE-inhibiting α -crystalline form of the tert-butylamine salt of perindopril

IN Pfeiffer, Bruno; Ginot, Yves-Michel; Coquerel, Gerard; Belles, Stephane

PA Les Laboratoires Servier, Fr.

SO PCT Int. Appl., 16 pp.

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
2001083439	A2	20011108	2001-FR2169	20010706

(preparation and X-ray characterization of the ACE-inhibiting α -crystalline form of the tert-butylamine salt of perindopril)

RN 107133-36-8 CAPLUS

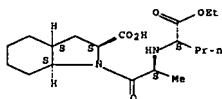
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

LA ANSWER 153 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

IN 2001:816626 CAPLUS [Full-text](#)

DN 135:344373

TI Process for preparing the novel γ crystalline form of the diuretic perindopril tert-butylamine salt

IN Pfeiffer, Bruno; Ginot, Yves-Michel; Coquerel, Gerard; Belles, Stephane

PA Adir et Compagnie, Fr.

SO PCT Int. Appl., 11 pp.

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
2001083439	A2	20011108	2001-FR2169	20010706

PI MO 2001087835 A1 20011122 WO 2001-FR2167 20010706

N: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NZ, OL, OM, OS, PA, PE, PG, PH, PK, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, SM, SN, SV, TC, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RM: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, NG, SN, TD, TG

FR 2811320 A1 20020111 FR 2000-8793 20000706

FR 2811320 B1 20020823

CA 2415438 A1 20011122 CA 2001-2415438 20010706

EP 1296947 A1 20030402 EP 2001-954058 20010706

EP 1296947 B1 20040204

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, NG, SN, TD, TG

BR 2001012367 A 20030513 BR 2001-12367 20010706

JP 2003533507 T 20031111 JP 2001-584232 20010706

JP 3602826 B2 20041215

AT 258918 T 20040215 AT 2001-954058 20010706

NZ 523173 A 20040430 NZ 2001-523173 20010706

PT 1296947 T 20040531 PT 2001-954058 20010706

ES 200300001 A 20040816 ES 2001-1 20010706

ES 2214434 T3 20040916 ES 2001-1954058 20010706

AP 1537 A 20060228 AP 2002-2691 20010706

M: GM, GH, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW

CZ 297672 B6 20070228 CZ 2003-357 20010706

SK 285714 B6 20070607 SK 2003-149 20010706

IN 2002MU00597 A 20040417 IN 2002-MU597 20020703

ZA 2002010092 A 20031212 ZA 2002-10092 20021212

IN 2002MN01815 A 20050204 IN 2002-MN1815 20021216

MX 2002PA12949 A 20030515 MX 2002-PA12949 20021219

US 2003186896 A1 20031002 US 2002-312961 20021231

NO 2003000024 A 20030103 NO 2003-04 20030103

NO 323447 B1 20070507

BG 107532 A 20031231 BG 2003-107532 20030205

BG 64868 B1 20060731

HR 2003000077 A 20030430 HR 2003-77 20030206

US 2005059609 A1 20050317 ~~US 2004-792355~~ 20040303

JP 2005047902 A 20050224 JP 2004-206158 20040713

IN 2004MN0628 A 20060707 IN 2004-MN628 20061104

IN 2005MU00129 A 20060901 IN 2005-MU129 20060208

SG 125975 A1 20061030 SG 2005-1530 20050311

AU 2006101079 A5 20070118 AU 2006-101079 20061222

AU 2007203451 A1 20070816 AU 2007-203451 20070725

PRAI FR 2000-8793 A 20000706

JP 2001-584232 A3 20010706

WO 2001-FR2167 W 20010706

IN 2002-MU597 A3 20020703

IN 2002-MN1815 A3 20021216

US 2002-312961 B1 20021231

AB The α -crystalline form of the ACE-inhibiting tert-butylamine salt of perindopril is prepared by refluxing the tert-butylamine salt of perindopril in Et acetate, cooling the mixture, and filtering the α -crystal modification, which is characterized by its powder X-ray diffraction pattern, and a I-containing pharmaceutical formulation is prepared

IT 107133-36-8, Perindopril erbumine

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

MO 2001083439 A3 20020207

N: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NZ, OL, OM, OS, PA, PE, PG, PH, PK, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, SM, SN, SV, TC, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RM: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, NG, SN, TD, TG

FR 2811318 A1 20020111 FR 2000-8791 20000706

FR 2811318 B1 20020823

CA 2415447 A1 20011108 CA 2001-2415447 20010706

AU 200176420 A 20011112 AU 2001-76420 20010706

EP 1296948 A2 20030402 EP 2001-954060 20010706

EP 1296948 B1 20030910

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, NG, SN, TD, TG

BR 2001012211 A 20030506 BR 2001-12211 20010706

AT 249435 T 20030915 AT 2001-954060 20010706

JP 2003531890 T 20031028 JP 2001-580868 20010706

JP 3592296 B2 20041124

PT 1296948 T 20031231 PT 2001-954060 20010706

ES 2206423 T3 20040516 ES 2001-1954060 20010706

NZ 523311 A 20040625 NZ 2001-523311 20010706

EE 200300003 A 20040816 EE 2003-3 20010706

AP 1452 A 20050930 AP 2002-2709 20010706

M: GM, GH, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW

IN 2002MU00593 A 20040417 IN 2002-MU593 20020703

MX 2002PA12904 A 20030922 MX 2002-PA12904 20021219

IN 2002MN01893 A 20050204 IN 2002-MN1893 20021230

US 2003158121 A1 20030821 US 2002-312903 20021231

ZA 2003000025 A 20040210 ~~ZA 2003-25~~ 20030102

NO 2003000051 A 20030106 NO 2003-51 20030106

NO 323445 B1 20070507

BG 107534 A 20031231 BG 2003-107534 20030205

HR 2003000078 A1 20030430 HR 2003-78 20030206

HR 2003000078 B1 20040630

US 2004248817 A1 20041209 US 2004-811727 20040329

JP 2005002120 A 20050106 JP 2004-206157 20040713

SG 125976 A1 20061030 SG 2005-1531 20050311

IN 2005MN00362 A 20050923 IN 2005-MN362 20050502

PRAI FR 2000-8791 A 20000706

JP 2001-580868 A3 20010706

WO 2001-FR2167 W 20010706

IN 2002-MN1893 A3 20021230

US 2002-312903 B1 20021231

AB The γ crystalline form of the diuretic perindopril tert-butylamine salt (I) is prepared by refluxing a chloroform-I solution, cooling the solution to 0°, and filtering the I γ crystal modification which is characterized by its X-ray diffraction pattern; a I-containing formulation is presented.

IT 107133-36-8

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(process for preparing the novel γ crystalline form of the diuretic perindopril tert-butylamine salt)

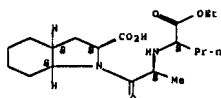
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd.

CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMP C4 H11 N

✓ ANSWER 164 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:597957 CAPLUS [Full-text](#)

DN 135:167034

TI Method for synthesis of perindopril and its pharmaceutically acceptable salts

IN Langlois, Pascal; Turbe, Hugues

PA Adir et Compagnie, Fr.

SO PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001058868	A1	20010816	WO 2001-FR1026	20010405
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RM:	GH, GM, KE, LS, MN, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,			

IT 107133-36-8P
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(method for synthesis of perindopril)

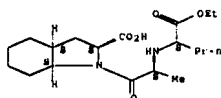
RN 107133-36-8 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMP C4 H11 NIT 122454-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for synthesis of perindopril)

RN 122454-52-8 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

BJ, CF, CG, CI, CM, GA, GM, GW, ML, MR, NE, SN, TD, TG				
FR 2807431	A1	20011012	FR 2000-4379	20000406
FR 2807431	B1	20020719		
HU 2001001336	A2	20020228	HU 2001-1336	20010330
HU 2001001336	A3	20030328		
CA 2405466	A1	20010816	CA 2001-2405466	20010405
AU 200148470	A	20010820	AU 2001-48470	20010405
EP 1268424	A1	20030102	EP 2001-921486	20010405
EP 1268424	B1	20070808		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR 2001009836	A	20030624	BR 2001-9836	20010405
JP 200351825	T	20031028	JP 2001-558419	20010405
JP 3939553	B2	20070704		
NZ 521454	A	20040326	NZ 2001-521454	20010405
EE 200200575	A	20040415	EE 2002-575	20010405
AP 1385	A	20050408	AP 2002-2630	20010405
AT 369338	T	20070815	AT 2001-921486	20010405
IN 2002MU00598	A	20040417	IN 2002-MU598	20020703
ZA 2002007419	A	20030916	ZA 2002-7419	20020916
IN 2002MN01284	A	20040703	IN 2002-MN1284	20020918
US 2003069431	A1	20030410	US 2002-239129	20020919
US 6635843	B2	20041228		
MX 2002PA09706	A	20040906	MX 2002-PA9706	20021002
NO 2002004808	A	20021004	NO 2002-4808	20021004
NO 324174	B1	20070903		
BG 107249	A	20030731	BG 2002-107249	20021104
HK 1053309	A1	20070511	HK 2003-105542	20030801
PRAI FR 2000-4379	A	20000406		
WO 2001-FR1026	W	20010405		

OS CASREACT 135:167034

AB Perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] was prepared by coupling (2S,3aS,7aS)octahydroindole-2-carboxylic acid tosylate with N-[(S)-1-carbethoxybutyl]-[(S)-alanine, followed by catalytic hydrogenation to remove the benzyl group. In an example, the coupling reaction was carried out in Et acetate in the presence of Et3N, 1-hydroxybenzotriazole and dicyclohexylcarbodiimide at 30° for 3h to give 92% perindopril benzyl ester.

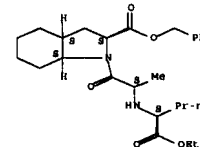
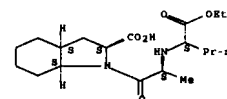
IT 42424-16-0P, Perindopril

RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for synthesis of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ ANSWER 165 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:581830 CAPLUS [Full-text](#)

DN 135:137713

TI Synthesis of N-[(S)-1-carboxybutyl]-[(S)-alanine esters for synthesis of perindopril

IN Souvire, Jean-Claude; Renaud, Alain

PA Adir et Compagnie, Fr.

SO PCT Int. Appl., 14 pp.

CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

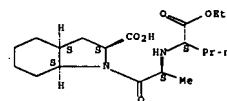
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001058972	A1	20010809	WO 2001-FR1088	20010410
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RM:	GH, GM, KE, LS, MN, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GM, GW, ML, MR, NE, SN, TD, TG			
FR 2807430	A1	20011012	FR 2000-4610	20000411
FR 2807430	B1	20020517		
HU 2001001337	A2	20011128	HU 2001-1337	20010330
HU 2001001337	A3	20021128		
CA 2405466	A1	20010809	CA 2001-2405466	20010410
CA 2405466	C	20050215		
EP 1272454	A1	20030108	EP 2001-923776	20010410
EP 1272454	B1	20070523		
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JP 2003518530	T	20030715	JP 2001-556822	20010410
JP 3872344	B2	20070124		
BR 2001009963	A	20030805	BR 2001-9963	20010410
EE 200200586	A	20040415	EE 2002-586	20010410
NZ 521846	A	20040730	NZ 2001-521846	20010410
AP 1417	A	20050524	AP 2002-2639	20010410
AT 362913	T	20070615	AT 2001-923776	20010410
IN 2002MU00595	A	20040417	IN 2002-MU595	20020703

10576386

305 of 361

ZA 2002007689 A 20030925 ZA 2002-7689 20020925
IN 2002001352 A 20040703 IN 2002-MN1352 20020930
NO 2002004811 A 20021004 NO 2002-4811 20021004
MX 2002PA09888 A 20040906 MX 2002-PA9888 20021007
US 2003109743 A1 20030612 US 2002-257239 20021009
US 6774259 B2 20040810
BG 107250 A 20030630 BG 2002-107250 20021104
HK 1053300 A1 20050401 HK 2003-105540 20030901
PRAI FR 2000-4610 A 20000411
WO 2001-FR1088 W 20010410
OS CASREACT 135:137713; MARPAT 135:137713
AB Title alanine deriva. (S)-R02CCHPr-L-Ala-OH (R = C1-C6 alkyl) were prepared by condensation of L-alanine with PrCOC2R under hydrogen pressure and 5% Pd/C as catalyst. In an example, hydrogenation of a mixture of 25 kg L-alanine, 1.1 kg soda and 36 kg Et 2-oxopentanoate in H2O over 5% Pd/C at room temperature and 1 bar pressure afforded N-[(S)-1-carboxybutyl]- (S)- alanine.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of [(carboxybutyl)alanine esters for synthesis of perindopril])
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 156 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
2001:581647 CAPLUS Full-text
DN 135:137711
TI Synthesis of N-[(S)-1-carboxybutyl]- (S)-alanine esters for synthesis of perindopril
IN Souvie, Jean-Claude
PA Adir et Compagnie, Fr.
SO PCT Int. Appl., 8 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2001056353 A2 20010809 WO 2001-FR959 20010330
WO 2001056353 A3 20020418
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,

10576386

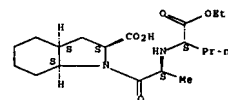
306 of 361

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FR 2807037 A1 20011005 FR 2000-4112 20000331
FR 2807037 B1 20020510
CA 2404700 A1 20010809 CA 2001-2404700 20010330
CA 2404700 C 20070220
AU 200148433 A 20010814 AU 2001-48433 20010330
HU 2001001335 A2 20011128 HU 2001-1335 20010330
HU 2001001335 A3 20021128
EP 1268398 A2 20030102 EP 2001-921440 20010330
EP 1268398 B1 20050608
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JP 2003534241 T 20031118 JP 2001-556065 20010330
JP 3930322 B2 20070613
BR 200109609 A 20040113 BR 2001-9609 20010330
NZ 521324 A 20040415 NZ 2001-521324 20010330
EE 200200553 A 20040415 EE 2002-553 20010330
AU 2001248433 B2 20041028 AU 2001-248433 20010330
AT 297377 T 20050615 AT 2001-921440 20010330
PT 1268398 T 20050930 PT 2001-921440 20010330
ES 2242743 T3 20051116 ES 2001-1921440 20010330
AP 1483 A 20051231 AP 2002-2628 20010330
W: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW
IN 2002MU00596 A 20040417 IN 2002-MU596 20020703
ZA 2002007150 A 20030905 ZA 2002-7150 20020905
IN 2002MU01255 A 20040624 IN 2002-MN1255 20020913
US 2003045744 A1 20030306 US 2002-221973 20020916
US 6818788 B2 20041116
MX 2002PA09378 A 20030212 MX 2002-PA9378 20020925
NO 2002004616 A 20020926 NO 2002-4616 20020926
BG 107234 A 20030731 BG 2002-107234 20021030
HK 1053301 A1 20050318 HK 2003-105541 20030801
PRAI FR 2000-4112 A 20000331
WO 2001-FR959 W 20010330
OS CASREACT 135:137711; MARPAT 135:137711
AB Title alanine deriva. (S)-R02CCHPr-L-Ala-OH (R = C1-C6 alkyl) were prepared by condensation of sodium pyruvate with (S)-R02CCHPrNH2.HCl under hydrogen pressure and 5% Pd/C as catalyst. In an example, hydrogenation of a mixture of 3 kg (S)-Et norvalinate hydrochloride and 2 kg sodium pyruvate in NaOH aqueous solution over 5% Pd/C at 35° and 1.2 bar pressure afforded 62% N-[(S)-1-carboxybutyl]- (S)-alanine.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of [(carboxybutyl)alanine esters for synthesis of perindopril])
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

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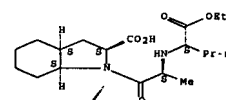
ANSWER 157 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
2001:338762 CAPLUS Full-text
DN 134:362293
TI Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
IN Farr, Spencer
PA Phase-1 Molecular Toxicology, USA
SO PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 200102928 A2 20010510 WO 2000-US0474 2001103
WO 200102928 A3 20020725
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NZ, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1999-165398 P 19991105
US 2000-1965719 P 20000411
AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predicted, to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.
IT 82834-16-0, Perindopril
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

10576386

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study, unclassified); BIOL (Biological study)
(methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



ANSWER 158 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN
2001:137173 CAPLUS Full-text
DN 134:178396
TI Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
IN Del Soldato, Piero
PA Nicox S.A., Fr.
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2001012584 A2 20010222 WO 2000-EP7225 20000727
WO 2001012584 A3 20020829
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MD, MK, MN, MX, NA, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
IT 99M1817 A1 20010212 IT 1999-M1817 19990812
CA 2381409 A1 20010222 CA 2000-2381409 20000727
BR 2000013264 A 20020416 BR 2000-13264 20000727
EP 1252133 A2 20021030 EP 2000-953102 20000727
EP 1252133 B1 20050608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
HU 2002003939 A2 20030328 HU 2002-3939 20000727
JP 2003515526 T 20030507 JP 2001-516885 20000727
CN 1433396 A 20030730 CN 2000-814049 20000727
NZ 516889 A 20041029 NZ 2000-516889 20000727
AU 781643 B2 20050602 AU 2000-65670 20000727
AT 297375 T 20050615 AT 2000-953102 20000727

10576386 309 of 361

EP 1593664 A1 20051109 EP 2005-104064 20000727
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, FI, RO, CY

RU 2264383 C2 20051120 RU 2002-103509 20000727
 ES 2243292 T3 20051120 ES 2000-95102 20000727
 NZ 535559 A 20051223 NZ 2000-535559 20000727
 CN 1923797 A 20070307 CN 2004-10136231 20000727
 ZA 2002000628 A 20030423 ZA 2002-628 20020123
 US 7186753 B1 20070306 US 2002-48469 20020207
 NO 2002000623 A 20020409 NO 2002-623 20020208
 MX 2002PA01519 A 20020702 MX 2002-PA1519 20020211
 AU 2002020824 A1 20050721 AU 2005-202824 20050628
 IN 2006CN01908 A 20070608 IN 2006-CN1908 20060530
 US 2007197499 A1 20070623 US 2006-642783 20061221

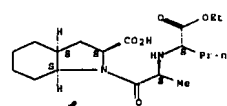
PRAI IT 1999-MI752 A 19990812
 CN 2000-951049 A3 20000727
 EP 2000-953102 A3 20000727
 IN 2002-CN147 A3 20000727
 WO 2000-EP7228 W 20000727
 US 2002-48469 A1 20020207

Compds. or their salts of general formula (I): A-B-N(O)s wherein: s is an integer equal to 1 or 2; A = R-T1-, wherein R is the drug radical and T1 = (CO) or (X) or (X)2, wherein X = O, S, NR1C, R1C is H or a linear or branched alkyl or a free valence, t and t' are integers and equal to zero or 1, with the proviso that t = 1 when t' = 0; t = 0 when t' = 1; B = -TB-X2-O- wherein TB = (CO) when t = 0, TB = X when t' = 0, X being as above defined; X2, bivalent radical, is such that the precursor drug of A and the precursor of B meet resp. the pharmacol. tests described in the description. Synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.

IT 82834-16-0, Perindopril
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (ACE-inhibitor); synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)

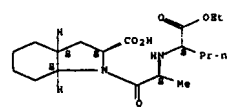
RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



AMSTER 159 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM
 2000:742057 CAPLUS Full-text
 133:309791

10576386 311 of 361
 Absolute stereochemistry. Rotation (-).



AMSTER 160 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM
 2000:742053 CAPLUS Full-text
 133:310142

Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

Del Soldato, Piero

PA Nicot S.A., Fr.

SO PCT Int. Appl., 159 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000061537	A2	20001019	WO 2000-EP3234	20000411
WO 2000061537	A3	20010927		
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KR, LC, LX, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RM: GH, GM, KE, LS, MM, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CP, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1311924	B1	20020320	IT 1999-MI753	19990413
CA 2370412	A1	20001019	CA 2000-2370412	20000411
BR 2000009702	A	20020108	BR 2000-9702	20000411
EP 1169294	A2	20020109	EP 2000-925203	20000411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002541233	T	20021203	JP 2000-610814	20000411
HU 2002003378	A	20030128	HU 2002-3378	20000411
NZ 514267	A	20040623	NZ 2000-514267	20000411
RU 2237657	C2	20041010	RU 2001-127576	20000411
AU 778989	B2	20041223	AU 2000-44001	20000411
ZA 2001008127	A	20030103	ZA 2001-8127	20011003
MX 2001PA10210	A	20020918	MX 2001-PA10210	20011009
NO 2001004927	A	20011213	NO 2001-4927	20011010
US 6989974	B1	20050323	US 2001-926326	20011015
US 2005261242	A1	20051124	US 2004-24857	20041230
PRAI IT 1999-MI753	A	19990413		
WO 2000-EP3234	W	20000411		
US 2001-926326	A3	20011015		

AMSTER 161 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STM
 2000:628026 CAPLUS Full-text
 133:322792

Combination therapy of angiotensin converting enzyme inhibitor and epoxy-steroidal aldosterone antagonist for treatment of cardiovascular disease

Alexander, John C.; Roniker, Barbara; Desai, Subhash

G.D. Searle and Co., USA

PCT Int. Appl., 212 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000051642	A1	20000908	WO 2000-US6633	20000303
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MY, NZ, OL, PG, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RM: GH, GM, KE, LS, MM, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CP, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2364169	A1	20000908	CA 2000-2364169	20000303
EP 1165136	A1	20020102	EP 2000-912174	20000303
EP 1165136	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

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Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

Del Soldato, Piero

Nicot S.A., Fr.

PCT Int. Appl., 140 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000061541	A2	20001019	WO 2000-EP3239	20000411
WO 2000061541	A3	20010927		

W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KR, LC, LX, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RM: GH, GM, KE, LS, MM, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CP, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

IT 1311923 B1 20020320 IT 1999-MI752 19990413
 CA 2370425 A1 20001019 CA 2000-2370425 20000411
 BR 2000009703 A 20020108 BR 2000-9703 20000411
 EP 1169298 A2 20020109 EP 2000-926870 20000411
 EP 1169298 B1 20060104

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JP 2002541236 T 20021203 JP 2000-610818 20000411
 TR 200102928 T2 20021223 TR 2001-2928 20000411
 HU 2002000714 A2 20021228 HU 2002-714 20000411

NZ 514270 A 20040227 NZ 2000-514270 20000411
 RU 2237057 C2 20040927 RU 2001-127574 20000411
 AU 778579 B2 20041021 AU 2000-45474 20000411

AT 315021 T 20060215 AT 2000-926870 20000411
 PT 1169298 T 20060531 PT 2000-926870 20000411
 ES 2256001 T3 20060716 ES 2000-926870 20000411

PL 193919 B1 20070430 PL 2000-350967 20000411
 ZA 2001008126 A 20030403 ZA 2001-8126 20011003
 MX 2001PA10213 A 20020918 MX 2001-PA10213 20011009

NO 2001004928 A 20011213 NO 2001-4928 20011010
 US 6987120 B1 20060117 US 2001-926322 20011015
 US 2006030605 A1 20060209 US 2005-234084 20050926

PRAI IT 1999-MI752 A 19990413
 WO 2000-EP3239 W 20000411
 US 2001-926322 A3 20011015

OS MARPAT 133:309791

Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.

IT 82834-16-0, Perindopril
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (ACE-inhibitor); synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

pharmacol. tests reported in the description; C and Cl are two bivalent radicals; the precursors of the radicals B and B1 are such as to meet the pharmacol. test reported in the description) were prepared for use as pharmaceuticals. Thus, (S,S)-N-acetyl-S-(6-methoxy-α-methyl-2-naphthalenylacetyl)cysteine 4-nitroxybutyl ester was prepared (NCX 2101) from naproxene and N-acetylcysteine in the first of 28 synthetic examples given. Pharmacol. test examples and tabular data are also given.

IT 82834-16-0, Perindopril
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (drug precursor)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

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 RL: RCT (Reactant); RACT (Reactant or reagent)
 (drug precursor)

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Absolute stereochemistry. Rotation (-).

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Absolute stereochemistry. Rotation (-).

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Absolute stereochemistry. Rotation (-).

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Absolute stereochemistry. Rotation (-).

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RN 82834-16-0 CAPLUS
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Absolute stereochemistry. Rotation (-).

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IT 82834-16-0, Perindopril
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (drug precursor)

RN 82834-16-0 CAPLUS
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Absolute stereochemistry. Rotation (-).

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IT 82834-16-0, Perindopril
 RL: RCT (Reactant); RACT (Reactant or reagent)
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RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

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 RL: RCT (Reactant); RACT (Reactant or reagent)
 (drug precursor)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

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313 of 361

TR 200102581 T2 20020422 TR 2001-2581 20000303
 BR 2000000781 A 20020702 BR 2000-8781 20000303
 HU 2002000519 A2 20030729 HU 2002-519 20000303
 JP 2002538172 T 20021112 JP 2000-602308 20000303
 AT 249242 T 20030915 AT 2000-912174 20000303
 EP 1382351 A1 20040121 EP 2003-19610 20000303
 EP 1382351 B1 20051123
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 PT 1165136 T 20040227 PT 2000-912174 20000303
 ES 2206204 T3 20040516 ES 2000-912174 20000303
 NZ 514205 A 20040730 NZ 2000-514205 20000303
 AU 778559 B2 20041209 AU 2000-33945 20000303
 AT 310537 T 20051215 AT 2003-19610 20000303
 ES 2250803 T3 20060416 ES 2003-3019610 20000303
 MX 2001PA09035 A 20040812 MX 2001-PA09035 20010905
 IN 2001CN01238 A 20050304 IN 2001-CN1238 20010905
 ZA 2001007779 A 20021220 ZA 2001-7779 20010920
 HK 1042252 A1 20040423 HK 2002-104154 20020531
 US 2004077611 A1 20040422 US 2003-440691 20030519
 US 2005250748 A1 20051110 US 2003-637070 20030806
 NZ 529635 A 20031219 NZ 2003-529635 20031119
 HK 1061200 A1 20060224 HK 2004-104294 20040614
 AU 2005201045 A1 20050407 AU 2005-201045 20050309
 PRAI US 1999-122977P P 19990305
 US 1999-122978P P 19990305
 EP 2000-912174 A3 20000303
 US 2000-518854 B1 20000303
 US 2000-518855 B1 20000303
 WO 2000-095633 W 20000303

AB Combinations of an ACE inhibitor and an epoxy-steroidal aldosterone receptor antagonist are described for use in treatment of circulatory disorders. Of particular interest are therapies using epoxy-steroidal-type aldosterone receptor antagonist compds., such as eplerenone, in combination with an angiotensin converting enzyme inhibitor. This co-therapy would be particularly useful to treat congestive heart failure while avoiding or reducing aldosterone-antagonist-induced side effects such as hyperkalemia. Capsules were prepared containing captopril 62.0 and eplerenone 12.5 mg/capsule.

IT 82834-16-0, S 5590

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (S 5590: combination therapy of angiotensin converting enzyme inhibitor and epoxy-steroidal aldosterone antagonist for treatment of cardiovascular disease)

RN 182176-83-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, mixt. with 3-(aminosulfonyl)-4-chloro-N-(2,3-dihydro-2-methyl-1H-indol-1-yl)benzamide (CA INDEX NAME)

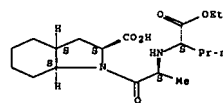
CM 1

CRN 82834-16-0
 CNF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

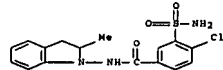
10576386

314 of 361



CM 2

CRN 26807-65-8
 CNF C16 H16 Cl N3 O3 S



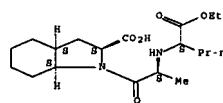
IT 82834-16-0, Perindopril

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (combination therapy of angiotensin converting enzyme inhibitor and epoxy-steroidal aldosterone antagonist for treatment of cardiovascular disease)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

18 ANSWER 163 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 2005191639 CAPLUS Full-text

DN 133.68211

TI Does Chinese ethnicity affect the pharmacokinetics and pharmacodynamics of angiotensin-converting enzyme inhibitors?

AU Ding, P. Y. A.; Hu, O. Yoa-Pu; Pool, P. E.; Liao, M.-C.

10576386

315 of 361

CS Department of Internal Medicine, Veterans General Hospital-Taipei, Taipei, Taiwan
 SO Journal of Human Hypertension (2000), 14(3), 163-170
 CODEN: JHHYEN; ISSN: 0950-9240
 PB Nature Publishing Group
 DT Journal; General Review
 LA English
 AB A review with 53 refs. Information from clin. and pharmacokinetic studies of angiotensin-converting enzyme inhibitors (ACEIs) has come from subjects who are mostly male and Caucasian, but the use of ACEIs extends to populations worldwide. Significant differences between Chinese in general and male Caucasians have been demonstrated in the pharmacokinetics/dynamics of other drug classes, and this could have implications for the use of ACEIs in the Chinese population. These include: significant Chinese/Caucasian genetic variation in the renin-angiotensin system based on an insertion/deletion polymorphism of the ACE gene; the genetic regulation of plasma ACE activity in the Chinese population; and genetic factors involving hypertension which may also influence the response to treatment. Oral and i.v. pharmacokinetic data from various studies of Chinese and Caucasian subjects are available for cilazapril, fosinopril, and perindopril, and pharmacodynamic data are available for eight different ACEIs. Based on these data, there are few differences in the pharmacokinetics of ACEIs between Chinese and Caucasians. Most ACEIs showed good blood-pressure-lowering efficacy in Chinese (benazepril, enalapril, fosinopril and spirapril), with perhaps less efficacy of cilazapril or a relatively shorter-term effect with cilazapril or perindopril, compared to Caucasians. Chinese experience more cough from ACEIs (captopril and enalapril) than Caucasians. Data suggest that fosinopril may not induce cough in as many subjects as do other ACEIs, and this seems to be true of Chinese as well. The mechanism, currently unknown, could involve fosinopril's dual elimination pathway (hepatic and renal). Pharmacokinetic data also support the use of fosinopril in congestive heart failure where elimination pathways may be impaired. In conclusion, ethnic differences between Chinese and Caucasians with respect to ACE and angiotensin gene polymorphisms, which might be expected to differentially affect the action of ACEIs in these two ethnic groups, do not, in fact, have such an effect. Rather, differences among the ACEIs appear to be more important.

IT 82834-16-0, Perindopril

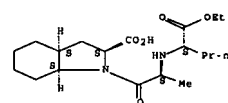
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(Chinese ethnicity effect on the pharmacokinetics and pharmacodynamics of angiotensin-converting enzyme inhibitors)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



10576386

316 of 361

RE.CNT 53

THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

18 ANSWER 163 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 1999599960 CAPLUS Full-text

DN 131.199561

TI Synthetic routes of perindopril

AU Chen, Ying-Wu; Chen, Jing

CS Wuhan College of Chemical Technology, Wuhan, 430074, Peop. Rep. China

SO Zhongguo Yiyao Gongye Zazhi (1999), 30(8), 382-384

CODEN: ZYGZEA; ISSN: 1001-6255

PB Zhongguo Yiyao Gongye Zazhi Bianjibu

DT Journal; General Review

LA Chinese

AB A brief review, with 16 refs., illustrating synthetic schemes for the preparation of perindopril.

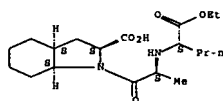
IT 82834-16-0, Perindopril

RL: PHU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (review of synthesis of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



18 ANSWER 164 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 199934890 CAPLUS Full-text

DN 130.100648

TI ACE inhibitor nitric acid salts

IN Del Soldato, Piero

PA Nicox S.A., Fr.

SO PCT Int. Appl., 21 pp.

CODEN: PIXX2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9900361	A1	19990107	WO 1998-EP3946	19980624
M: AL, AU, BB, BG, BR, CA, CN, CZ, DE, DK, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, TJ, TM				
RW: GW, GM, KE, LS, MW, SD, SE, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,				

CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2292794 A1 19990107 CA 1998-2292794 19980624
 AU 9887300 A 19990119 AU 1998-87300 19980624
 AU 740411 B2 20011101
 EP 1019370 A1 20000719 EP 1998-938668 19980624
 EP 1019370 B1 20030102

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO

HU 200003133 A2 20010328 HU 2000-3133 19980624
 HU 200003133 A3 20021028
 JP 2002506456 T 20020226 JP 1999-505294 19980624
 RU 2194027 C2 20021210 RU 2000-100825 19980624
 AT 230393 T 20030115 AT 1998-938668 19980624
 ES 2190095 T3 20030716 ES 1998-938668 19980624
 IL 132691 A 20040601 IL 1998-132691 19980624
 BR 9810459 A 20061003 BR 1998-10459 19980624
 US 6218417 B1 20010417 US 1999-423287 19991108

PRAI IT 1997-M11523 A 19970627
 MO 1997-EP3946 W 19980624

OS MARPAT 130/100648

AB The invention relates to products having an improved antihypertensive activity and fewer side effects, in particular in the bronchi. Nitric acid salts of ACE inhibitors show an antihypertensive activity combined with platelet-antaggregating activity. I.p. injection of enalapril nitrate at 100 or 300 µg/kg to rats with induced hypertension inhibited the symptoms by 35 and 67 %, vs. 18 and 55 % for enalapril maleate.

IT 219553-93-2 CAPLUS
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (ACE inhibitor nitric acid salts with improved antihypertensive effects)

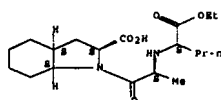
RN 219553-93-2 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, mononitrate (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 7697-37-2

CMF H N O3



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ ANSWER 165 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 1998-438838 CAPLUS Full-text

DN 129-174067

TI Possible participation of angiotensin-converting enzyme and of leukocyte

elastase in pathogenesis of non-insulin dependent diabetes mellitus

AU Dotenko, V. L.; Demidova, T. Yu.; Neshkova, E. A.; Ametov, A. S.;

Varovaya, G. A.

CS Ross. Med. Akad. Polediplomn. Obrazovaniya, Moscow, 123836, Russia

SO Voprosy Meditsinskoi Khimii (1998), 44(2), 203-212

CODEN: VMDKAM; ISSN: 0042-8809

PB NII Biomeditsinskoi Khimii

DT Journal

LA Russian

AB It is commonly accepted that the tolerance to insulin and hyperglycemia of the patients with non-insulin dependent diabetes mellitus (NIDDM) is due to some defect of insulin receptors or disturbances in the signaling pathway of the cell. This disease is often accompanied by hypertension. In this paper the high activity of plasma kallikrein-kinin system (KKS) (kallikrein activity was 6-8-fold higher than normal), of angiotensin-converting enzyme (ACE) (4-fold greater than normal), and of leukocyte elastase (2.7-fold higher than normal) were demonstrated in plasma of patients with NIDDM. Increased KKS activity was coincident with rising ACE activity, which may be the cause of the fast bradykinin inactivation and onset of hypertension. The treatment with ACE inhibitor during 3 mo (4 mg of Perindopril per day) decreased ACE activity in patients' plasma which was accompanied by decreased arterial pressure and some restoration of carbohydrate metabolism indicators. The hyperinsulinemic euglycemic clamping of 7 patients with NIDDM and essential hypertension showed that ACE-inhibitor (Perindopril, 4 mg) prevented bradykinin from destruction and increased the glucose consumption by tissues. The high activity of polyaromatic leukocytes and secretion of the elastase in NIDDM patients' plasma and/or instability of plasma and granular membranes of leukocytes in conditions of hyperglycemic plasma are probably the cause of endothelial irritation and high ACE secretion. Secondly, the leukocyte may be the cause of injury and decreased susceptibility of cell receptors for insulin and bradykinin.

IT 42524-16-0, Perindopril

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(participation of angiotensin-converting enzyme and of leukocyte

elastase in pathogenesis of non-insulin dependent diabetes mellitus)

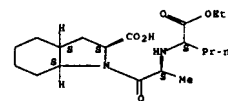
RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

✓ ANSWER 167 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 1995-55706 CAPLUS Full-text

DN 129-174119

TI A pharmaceutical product comprising a salicylate of an esterifiable

ACE-inhibitor

IN Byrne, William; Rynne, Andrew

PA Cal International Ltd., Ire.

SO PCT Int. Appl., 46 pp.

CODEN: PIXX22

DT Patent

LA English

PAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9520571	A1	19950803	WO 1995-IE12	19950127
R: AT, AU, BR, CA, CH, CN, DE, DK, ES, FI, GB, HU, JP, LU, NL, NO, PL, RO, RU, SE, US				
RM: AT, BE, CH, DE, DK, ES, FR, GB, IE, LU, SE, NE				
CA 2182198	A1	19950803	CA 1995-2182198	19950127
AU 9516709	A	19950815	AU 1995-16709	19950127
EP 741699	A1	19951113	EP 1995-908264	19950127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
GB 2300635	A	19961113	GB 1996-16297	19950127
GB 2300635	B	19980617		
JP 09509150	T	19970916	JP 1995-519969	19950127
ZA 9500703	A	19950929	ZA 1995-703	19950130
US 5852047	A	19981222	US 1996-682663	19960729
PRAI IE 1994-80	A	19940128		
WO 1995-IE12	A	19950127		

AB Salicylates of esterifiable ACE inhibitors, especially captopril-8-

aspartate, and processes for their preparation are described. A

pharmaceutical composition (e.g. capsules or tablets) contains the compds. of

the invention and may also contain a diuretic and K⁺ salts.

IT 82834-16-0, Perindopril

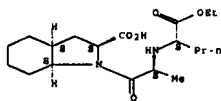
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of compns. containing salicylate of esterifiable ACE-

inhibitors)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA



✓ ANSWER 166 OF 186 CAPLUS COPYRIGHT 2007 ACS ON STN

AN 1977-44050 CAPLUS Full-text

DN 129-14334

TI Influence of the angiotensin II type 1 receptor gene polymorphism

on the effects of perindopril and nitrendipine on arterial stiffness in

hypertensive individuals

AU Benetos, Athanasios; Cambien, Francois; Gautier, Sylvie; Ricard, Sylvain;

Safar, Michel; Laurent, Stephane; Lacolley, Patrick; Poirier, Odette;

Topouchian, Jirar; Asmar, Roland

CS Broussais Hospital, Institut National de la Sante et de la Recherche

Medicale, Paris, 75014, Fr.

SO Hypertension (Dallas) (1996), 28(6), 1081-1084

CODEN: HPRTON; ISSN: 0194-911X

PB American Heart Association

DT Journal

LA English

AB Angiotensin-converting enzyme inhibitors improve arterial stiffness

independently of blood pressure reduction. Since the authors have recently

shown that in hypertensive individuals the A 1166C polymorphism of the

angiotensin II type 1 receptor (AT1-R) is an independent determinant of aortic

stiffness, the authors designed the present study to assess the influence of

this polymorphism on the changes of aortic stiffness after chronic treatment

with the angiotensin-converting enzyme inhibitor perindopril and the calcium

channel blocker nitrendipine. Forty perindopril- and 42 nitrendipine-treated

hypertensive individuals were studied. The authors evaluated aortic stiffness

by measuring the carotid-femoral pulse wave velocity. Carriers of the AT1-R C

allele showed higher baseline values of pulse wave velocity than AA

homozygotes. In the perindopril group, a threefold greater reduction in pulse

wave velocity was observed in carriers of the C allele than in AA homozygotes

(-2.85 vs. -0.94 m/s, resp.), whereas in the nitrendipine group, pulse wave

velocity decreased only in AA homozygotes and not in AT1-R C carriers (-1.38

vs. -0.04 m/s, resp.). These results indicate that according to the AT1-R A

1166C genotype, an angiotensin-converting enzyme inhibitor and a calcium

channel blocker affect pulse wave velocity in opposite ways. Since some

evidence shows that increased pulse wave velocity may enhance cardiovascular

risk, it might be useful for physicians to consider the AT1-R genotype when

prescribing an angiotensin-converting enzyme inhibitor or calcium channel

blocker to a hypertensive individual.

IT 82834-16-0, Perindopril

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)

(influence of angiotensin II type 1 receptor gene polymorphism

on effects of perindopril and nitrendipine on arterial stiffness in

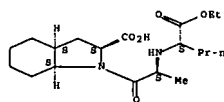
hypertensive humans)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-

INDEX NAME)

Absolute stereochemistry. Rotation (-).



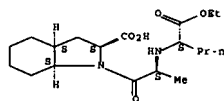
IT 82834-16-0D, Perindopril, aspirin derivs.

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of compns. containing salicylate of esterifiable ACE-inhibitors)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LA ANSWER 168 OF 186 CAPLUS COPYRIGHT 2007 ACS on STW

AN 993.73362 CAPLUS Full-text

DN 118:73362

TI Synthesis and ACE inhibitory activity of the stereoisomers of perindopril (S 9490) and perindoprilate (S 9780)

AU Vincent, Michel; Marchand, Bernard; Remond, Georges; Jaguelin-Guinamant, Sylvie; Damien, Gerard; Portevin, Bernard; Baumal, Jean Yves; Volland, Jean Paul; Bouchet, Jean Paul; et al.

CS Inst. Rech. Serv. 11, Suresnes, 92150, Fr.

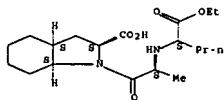
SO Drug Design and Discovery (1992), 9(1), 11-28

CODEN: DDDIEV; ISSN: 1055-9612

DT Journal

LA English

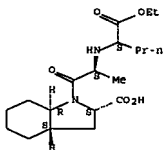
GI

I, R=E
II, R=H

RN 145513-30-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3αβ,7αα]]- (9CI)
(CA INDEX NAME)

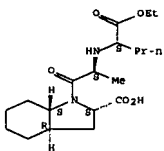
Absolute stereochemistry.



RN 145513-31-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3αα,7αβ]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 145513-32-2 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3αα,7αα]]- (9CI)
(CA INDEX NAME)

Preindopril, a powerful ACE (angiotensin converting enzyme) inhibitor contains 5 chiral carbons, and thus there is the possibility of 25 - 32 stereoisomers for the general structure I. These 32 stereoisomers were prepared by crosscoupling the 8 stereoisomers of benzyl perhydroindole-2- carboxylate with the 4 stereoisomers of 2-(1-carbethoxybutylamino)propionic acid, and hydrogenating the resulting benzyl esters. Each stereoisomer of perindopril furnished by saponification of the corresponding diacid stereoisomer (II) of perindoprilate which is the active form of perindopril. For each of the 32 stereoisomers of II, the in vitro ACE inhibitory potency was determined. Four of them, including perindoprilate, had activities in the nanomolar range, and 4 more were ca. 10-fold less active. The 4 acid esters of I corresponding resp. to the 4 most active diacids II, in vitro were studied (1 mg/kg via the oral route) for their in vivo activity in dogs. The oral absorption of the active acid esters I and their activation to the active diacid II depended only on the chiralities of the 2 ring junction carbons of the perhydroindole ring.

IT 82834-16-0DP, Perindopril, isomers 82834-16-0P

145513-30-0P 145513-31-1P 145513-32-2P

145513-33-3P 145513-34-4P 145513-35-5P

145513-36-6P 145513-37-7P 145513-38-8P

145513-39-9P 145513-40-2P 145513-41-3P

145513-42-4P 145513-43-5P 145513-44-6P

145513-45-7P 145513-46-8P 145513-47-9P

145513-48-0P 145513-49-1P 145513-50-4P

145513-51-5P 145513-52-6P 145513-53-7P

145513-54-8P 145513-55-9P 145513-56-0P

145513-57-1P 145513-58-2P 145513-59-3P

145513-94-4P

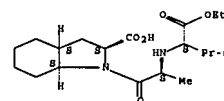
RL: SPW (Synthetic preparation); PEEF (Preparation)

(preparation and angiotensin I-converting enzyme inhibitory activity of, chirality-structure activity in relation to)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

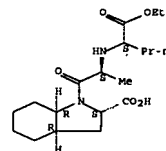


RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

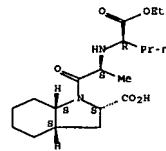
Absolute stereochemistry.



RN 145513-33-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2α,3αβ,7αβ]]- (9CI)
(CA INDEX NAME)

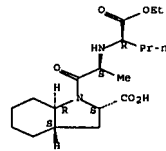
Absolute stereochemistry.



RN 145513-34-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2α,3αβ,7αα]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

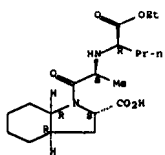


10576386

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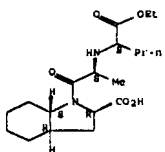
RN 145513-35-5 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1(R*(S*)),2 α ,3 α ,7 α]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



RN 145513-36-6 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1(S*(S*)),2 α ,3 α ,7 α]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.

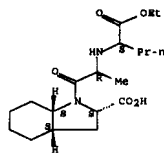


RN 145513-37-7 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1(S*(R*)),2 α ,3 α ,7 α]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.

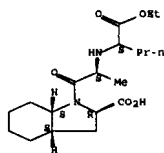
10576386

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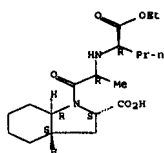
RN 145513-38-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1(S*(S*)),2 α ,3 α ,7 α]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



RN 145513-39-9 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1(S*(S*)),2 α ,3 α ,7 α]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



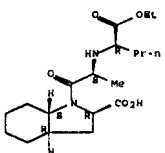
RN 145513-40-2 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-

10576386

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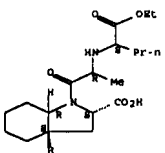
oxopropyl]octahydro-, [2R-[1(S*(R*)),2 α ,3 α ,7 α]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



RN 145513-41-3 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1(S*(R*)),2 α ,3 α ,7 α]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.

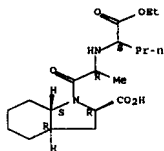


RN 145513-42-4 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1(R*(S*)),2 α ,3 α ,7 α]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.

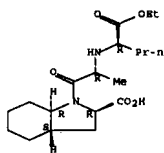
10576386

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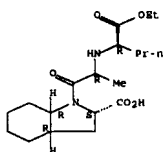
RN 145513-43-5 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1(R*(R*)),2 α ,3 α ,7 α]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



RN 145513-44-6 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1(S*(S*)),2 α ,3 α ,7 α]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



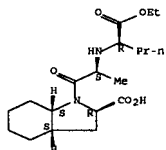
RN 145513-45-7 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-

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oxopropyl]octahydro-, [2R-[1[S*(R*)],2 α ,3 α ,7 α]]- (9CI)
(CA INDEX NAME)

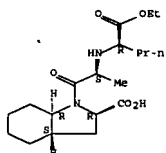
Absolute stereochemistry.



RN 145513-46-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(R*)],2 α ,3 α ,7 α]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 145513-47-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2 α ,3 α ,7 α]]- (9CI)
(CA INDEX NAME)

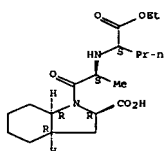
Absolute stereochemistry.

10576386

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oxopropyl]octahydro-, [2R-[1[S*(S*)],2 α ,3 α ,7 α]]- (9CI)
(CA INDEX NAME)

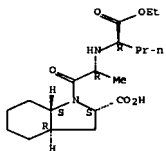
Absolute stereochemistry.



RN 145513-51-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(S*)],2 α ,3 α ,7 α]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



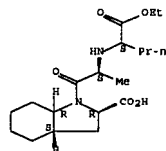
RN 145513-52-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(S*)],2 α ,3 α ,7 α]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

10576386

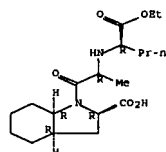
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RN 145513-48-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R,3 α ,7 α]- (9CI)
(CA INDEX NAME)

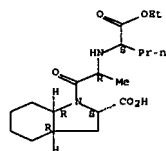
Absolute stereochemistry.



RN 145513-49-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(R*)],2 α ,3 α ,7 α]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

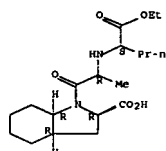


RN 145513-50-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-

10576386

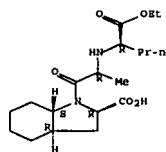
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RN 145513-53-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(R*)],2 α ,3 α ,7 α]]- (9CI)
(CA INDEX NAME)

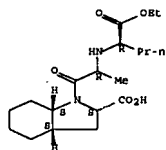
Absolute stereochemistry.



RN 145513-54-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(S*)],2 α ,3 α ,7 α]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

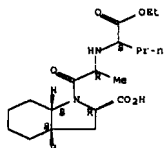


RN 145513-55-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2R,3aS,7aS)- (9CI)
(CA INDEX NAME)

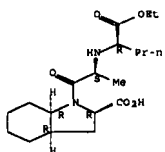
Absolute stereochemistry.



RN 145513-56-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(R*)],2α,3αβ,7αβ]]- (9CI)
(CA INDEX NAME)

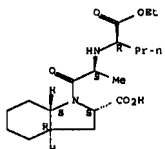
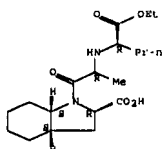
Absolute stereochemistry.



RN 145513-57-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(R*)],2α,3α,7α]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



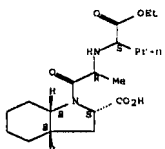
IT 120782-54-4P

RL: SPH (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 130982-52-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2S-[1[S*(R*)],2α,3αβ,7αβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



• HCl

LV NUMBER 169 OF 166 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1992-612157 CAPLUS [Full-text](#)

DN 117-212157

TI Preparation and formulation of [(mercaptoalkyl)carbamoyl]benzoates as analgesic and cardiovascular agents

IN Neustadt, Bernard R.

PA Schering Corp., USA

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

PAN.CNT 1

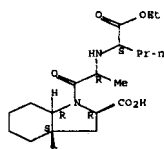
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9211235	A1	1992-07-09	WO 1991-US9189	1991-12-19

W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MM, PL, RO,

RN 145513-58-2 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(S*)],2α,3α,7αβ]]- (9CI)
(CA INDEX NAME)

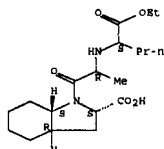
Absolute stereochemistry.



RN 145513-59-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(R*)],2α,3α,7αβ]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 145513-94-6 CAPLUS

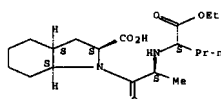
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2α,3α,7αβ]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



SD, SU, US
RN: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG
US 5232920 A 19930803 US 1990-633696 19901221
AU 9191046 A 19920722 AU 1991-91046 19911219
ZA 9110014 A 19920826 ZA 1991-10014 19911219
EP 563153 A1 19931006 EP 1992-901485 19911219
EP 563153 B1 19950315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE
JP 05509331 T 19931222 JP 1992-501584 19911219
AT 119879 T 19950415 AT 1992-901485 19911219
ES 2072138 T3 19950701 ES 1992-901485 19911219
PRAI US 1990-633696 A2 19901221
WO 1991-US9189 A 19911219
OS MARPAT 117-212157
AB R5CH2CH[(CH2)mR1]NHCOR2 [R = H, CHO, alkanoyl, aroyl; R1 = (cyclo)alkyl, (hetero)aryl; R2 = ZCOR3, (substituted) heteroaryl; R3 = OH, (substituted) alkoxy, -amino; Z = (substituted) arylene; m = 1, 2] were prepared. Thus, (S)-2-MeC6H4CH2CH(CH2SAC)CO2H was treated with (PhO)2P(O)N3 and Et3N in PhMe and the product condensed with PhCH2OH to give, after HBr/HOAc treatment, (R)-2-MeC6H4CH2CH(NH2)CH2SAC.HBr which was condensed with 3-(MeO2C)C6H4COCl to give, after saponification, (R)-2-MeC6H4CH2CH(CH2SH)NHCOC6H4(CO2H)-3. The latter gave 47 mmHg drop in blood pressure in exptl. hypertensive rats at 1 mg/kg orally.
IT 32824-16-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(comps. containing [(mercaptoalkyl)carbamoyl]benzoates and, as cardiovascular agents)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[1(S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LV NUMBER 170 OF 166 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1992-114770 CAPLUS [Full-text](#)

DN 116-14770

TI Preparation of disulfide derivatives of mercaptoacylamino acids as cardiovascular agents

IN Haslanger, Martin F.; Neustadt, Bernard R.; Smith, Elizabeth M.

PA Schering Corp., USA

SO PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DT Patent

LA English

PAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9117980	A1	19911128	WO 1991-US3251	19910515
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 9179572	A	19911210	AU 1991-79572	19910515
ZA 9103685	A	19920226	ZA 1991-3685	19910515
EP 528997	A1	19930303	EP 1991-911546	19910515
EP 528997	B3	19950201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05502038	T	19930415	JP 1991-510190	19910515
JP 06102648	B	19941214		
ES 2069893	T3	19950516	ES 1991-911546	19910515
US 1990-525370	A2	19900517		
WO 1991-US3251	A	19910515		

OS MARPAT 116:174770

AB [SCH2CH(CH2R1)NCONHCHR2CHR4(CH2)t(CHR9)PCOR3]2, [SCH2CH(CH2R7)NCONHCHR2COR3] (R1 = alkyl, cycloalkyl, aryl, heteroaryl; R2 = H, alkyl, cycloalkyl, hydroxyalkyl, alkoxy, HS, alkythio, aryl, heteroaryl, aralkyloxy, aralkylthio, R3 = R5O, R5R6M, R5, R6 = H, alkyl, hydroxyalkyl, etc., R5R6M = 5-7-membered ring; R4, R9 = (CH2)qR8, R8 = H, HO, alkoxy, HS, alkythio, aryl, heteroaryl; R7 = (substituted) Ph; n = 1, 2; p, t = 0, 1; q = 0-2) useful in treatment of cardiovascular disorders and pain, are prepared To N-[3-mercaptopropyl]-2-(2-methylbenzyl)propionyl]- (S)- methionine Et ester (preparation given) in absolute EtOH was added iodine/EtOH to give 1,1'-[dithiobis(2(S)-(2-methylbenzyl)-1-oxo-3,1-propanediyl)]bis-(S)- methionine di-Et ester, which produced a drop in pressure in the DOCA salt model in the atrial natriuretic factor potentiation procedure. Pharmaceutical formulations containing the title compds. are given.

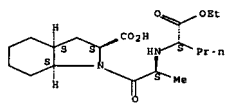
IT 82834-16-0, Perindopril

RL: RCT (Reactant); RACT (Reactant or reagent) (pharmaceutical containing mercaptoacylamino acid disulfide and)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

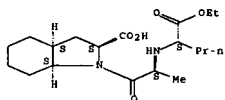


LS ANSWER 171 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 92:120263 CAPLUS Full-text

DN 16:120263

TI A new radioimmunoassay for the determination of the angiotensin-converting enzyme inhibitor Perindopril and its active metabolite in plasma and urine: advantages of a lysine derivative as immunogen to improve the



LS ANSWER 172 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1991:74706 CAPLUS Full-text

DN 114:74706

TI Configuration and preferential solid-state conformations of perindoprilat (S-9780). Comparison with the crystal structures of other ACE inhibitors and conclusions related to structure-activity relationships

AU Pascard, Claudine; Guilhem, Jean; Vincent, Michel; Remond, Georges; Portevin, Bernard; Laubie, Michel

CS Inst. Chim. Subst. Nat., Gif-sur-Yvette, 91198, Fr.

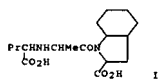
SO Journal of Medicinal Chemistry (1991), 34(2), 663-9

CODEN: JMCMAH; ISSN: 0022-2623

DT Journal

LA English

GI



AB The conformational of perindoprilat (I), an antihypertensive drug, is studied in the solid state by X-ray anal. The resolution of its structure reveals important analogies between its observed conformation and that of several angiotensin-converting enzyme (ACE) inhibitors of the same family. This comparison points out a constant relative orientation of the functional groups, regardless of the mol. environment. This angular constancy appears not to be accidental and is a good argument for the spatial design of the ACE binding site. Although ACE is a carboxy dipeptidase, the binding site may not contain two but one unique hydrophobic pocket receiving the C-terminal end of the inhibitors.

IT 82834-16-0, Perindopril

RL: RCT (Reactant); RACT (Reactant or reagent) (saponification of)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

assay specificity

AU Van den Berg, H.; Resplandy, G.; De Bie, A. T. H. J.; Floor, W.; Bertrand, M.; Arts, C. J. M.

CS CIVO Toxicol. Nutr. Inst., TNO, Zeist, 3700 AJ, Meth.

SO Journal of Pharmaceutical and Biomedical Analysis (1991), 9(7), 517-24

CODEN: JPBADA; ISSN: 0731-7085

DT Journal

LA English

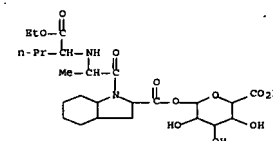
AB A new RIA was developed for the direct measurement of perindoprilat (PT), the active metabolite (diacid) of Perindopril (P), an angiotensin-converting enzyme (ACE) inhibitor. Antibodies were raised in rabbits against the lysine derivative of PT conjugated to bovine serum albumin. The p-hydroxyphenyl derivative of the lysine analog was used for preparation of the radioligand by iodination (125I). Cross-reactivities for the glucuronide metabolites of P and PT are low (0.25 and 3.5%, resp.). The theor. limit of detection is 0.2 nM, the sensitivity attainable with random samples is about 0.5 nM. Within- and between-assay variabilities observed were 4.2-6.7 and 2.8-5.9%, resp. (concentration range 2.1-41.7 nM). Serial dilution of plasma and urine samples showed excellent parallelism (r > 0.95). Recoveries of PT spiked to urine and plasma samples were 90-120%. The prodrug P can be measured in the same sample (plasma/urine) after chromatog. separation on a Dowex AG 1 x 2 anion-exchange column and quant. alkaline hydrolysis of the P-containing fraction. It is concluded that the specificity and sensitivity of this assay are amply sufficient for pharmacokinetic studies and in patient monitoring.

IT 120398-66-5

RL: ANST (Analytical study) (cross-reactivity of, in RIA for determination of perindopril and its metabolite)

RN 120398-66-5 CAPLUS

CN β-D-Glucopyranuronic acid, 1-[1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate], [2S-[1(R*(R*))],2α,3αβ,7αβ]]- (9CI) (CA INDEX NAME)



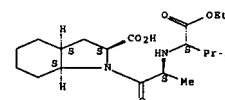
IT 82834-16-0, S-9490

RL: ANT (Analytical study) (determination of, in blood plasma and urine, by RIA)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LS ANSWER 173 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1990:584168 CAPLUS Full-text

DN 113:184168

TI Interspecies comparison of the metabolic pathways of perindopril, a new angiotensin-converting enzyme (ACE) inhibitor

AU Grislain, L.; Mocquard, M. T.; Dabe, J. P.; Bertrand, M.; Luijten, W.; Marchand, B.; Resplandy, G.; Devissaguet, M.

CS Bio-Pharm. Serv., Orleans, 45000, Fr.

SO Xenobiotica (1990), 20(8), 787-800

CODEN: XENOBH; ISSN: 0049-8254

DT Journal

LA English

AB

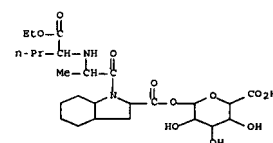
The metabolism of perindopril (non-thiol angiotensin-converting enzyme inhibitor) was studied in rat, dog and monkey after single oral and i.v. administration of 14C-perindopril, and in man after a single oral dose. Six biotransformation in all species is the hydrolysis of the carboxylic Et ester side-chain, with the formation of perindoprilate, the active metabolite. A minor route of biotransformation led to the acyl glucuronides of perindopril and perindoprilate. Internal dehydration of perindopril and perindoprilate into cyclic lactam structures occurs. This route of metabolism is of minor importance except in humans.

IT 120398-66-5

RL: FORM (Formation, nonpreparative) (formation of, as perindopril metabolite, in humans and laboratory animals)

RN 120398-66-5 CAPLUS

CN β-D-Glucopyranuronic acid, 1-[1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate], [2S-[1(R*(R*))],2α,3αβ,7αβ]]- (9CI) (CA INDEX NAME)

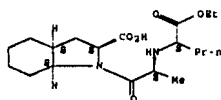


IT 82834-16-0

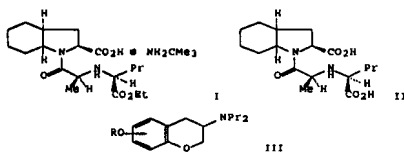
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(metabolism of, in humans and laboratory animals)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aB)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



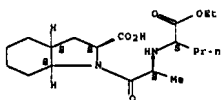
LE ANSWER 174 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1989:518595 CAPLUS Full-text
DN 111:134746
TI Some syntheses of tritium biochemicals at high specific radioactivity; radiosyntheses of ACE inhibitors, 5-HT1A and dopamine receptors radioligands
AU Pichat, L.
CS CEA - CEN Saclay, Gif-sur-Yvette, 91191, Fr.
SO Synth. Appl. Isot. Labelled Cpd. 1988, Proc. Int. Symp. (1989), Meeting Date 1988, 21-6. Editor(s): Baillie, Thomas A.; Jones, John Richards. Publisher: Elsevier, Amsterdam, Neth.
CODEN: S6OXA8
DT Conference
LA English
OI



AB A lecture with 9 refs. Synthesis of tritium labeled biochems. I and II as potent inhibitors of angiotensin converting enzyme (ACE) and III (OR = 5-OMe, 8-OMe) as D2 receptors is described.
IT 125650-71-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as angiotensin converting enzyme inhibitors)

enzyme inhibitor)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aB)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LE ANSWER 176 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1989:514746 CAPLUS Full-text
DN 111:134746
TI Preparation of N-[(alkoxycarbonyl)alkyl]-L-alanines as intermediates for carboxyalkyl dipeptides
IN Vincent, Michel; Ballearda, Jean; Marchand, Bernard; Remond, Georges
PA ADIR, Fr.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA French
FAM.CMT 1

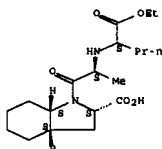
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 308340	A1	19890322	EP 1988-402338	19880916
EP 308340	B1	19910313		
R1: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2620699	A1	19890324	FR 1987-12901	19870917
FR 2620699	B1	19900601		
CA 1340870	C	19950601	CA 1988-577077	19880907
DK 8805150	A	19890318	DK 1988-5150	19880915
DK 172008	B1	19970915		
AU 8822355	A	19890323	AU 1988-22355	19880916
AU 606992	B2	19910221		
JP 01110652	A	19890427	JP 1988-232124	19880916
JP 06099073	B	19941207		
ZA 8806930	A	19890530	ZA 1988-6930	19880916
US 4902817	A	19900220	US 1988-245353	19880916
AT 61546	T	19910315	AT 1988-402338	19880916
ES 2023451	T3	19930316	ES 1988-402338	19880916
PRAI: FR 1987-12901	A	19870917		
EP 1988-402338	A	19880916		
GB CABREACT 111:134746; MARPAT 111:134746				
OI				

RN 125650-71-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, labeled with tritium, [2S-[1R*(R*)],2a,3aB,7aB]]-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 125650-70-6
CMF C19 H32 N2 O5
CIL XH-13

Absolute stereochemistry.

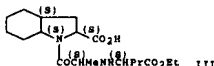


CM 2

CRN 75-64-9
CMF C4 H11 N

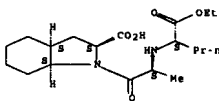


LE ANSWER 175 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1989:586736 CAPLUS Full-text
DN 111:186736
TI Modeling, synthesis, and pharmacology of perindopril (S-9490), an inhibitor of angiotensin I-converting enzyme
AU Vincent, Michel; Schiavi, Pierre
CS Inst. Rech., SERVIER, Suresnes, 92150, Fr.
SO Colloque INSERM (1989), 181 (Mec. Reconnaissance Mol.), 95-135
CODEN: CINMOR; ISSN: 0768-3154
DT Journal; General Review
LA French
AB A review with 4 refs.
IT 82834-16-0P, S-9490
RL: SPN (Synthetic preparation); PREP (Preparation)
(modeling and preparation and pharmacol. of, as angiotensin-converting



AB The title compds., (S,S)-HO2CCHMeNHCH(R1)CO2R2 (I, R1 = alkyl; R2 = H, alkyl), useful as intermediates for carboxyalkyl dipeptides R3CO-Q-COCHMeNHCH(R2) (II; R3 = H, alkyl; Q = a residue of indoline, isoindoline, tetrahydroquinoline, perhydroindole, perhydroisoindole, perhydroisoquinoline, etc.), notably perindopril (III), an antihypertensive, are prepared via esterification of (S)-H2NCH(R1)CO2H (IV) with R2OH and reaction of the resulting (S)-H2NCH(R1)CO2R2 with pyruvic acid under catalytic hydrogenation conditions. (S)-H2NCH(R1)CO2R2 (preparation given) was reacted with pyruvic acid under hydrogenation in the presence of Pd/C to give (S,S)-HO2CCHMeNHCH(R1)CO2R2.
IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediate for, N-[(ethoxycarbonyl)butyl]alanine as)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aB)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



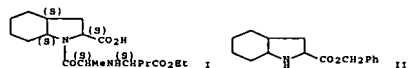
LE ANSWER 177 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1989:515749 CAPLUS Full-text
DN 111:134746
TI Preparation of perindopril via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine
IN Vincent, Michel; Ballearda, Jean; Marchand, Bernard; Remond, Georges
PA ADIR, Fr.
SO Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DT Patent
LA French
FAM.CMT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 308341	A1	19890322	EP 1988-402339	19880916
EP 308341	B1	19901212		
R1: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2620709	A1	19890324	FR 1987-12896	19870917

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FR 2620709 B1 19900907
 CA 1336348 C 19950718 CA 1988-577078 19880907
 DK 8805151 A 19890318 DK 1988-5151 19880915
 DK 171470 B1 19961111
 AU 8822362 A 19890323 AU 1988-22362 19880916
 AU 608363 B2 19910328
 JP 01110696 A 19890427 JP 1988-232125 19880916
 JP 05043717 B 19930702
 ZA 8806932 A 19890530 ZA 1988-6932 19880916
 US 4914214 A 19900403 US 1988-245446 19880916
 AT 59047 T 19901215 AT 1988-42339 19880916
 CA 1338015 C 19960130 CA 1991-616239 19911128
 PRAI FR 1987-12896 A 19870917
 CA 1988-577078 A3 19880907
 EP 1988-402339 A 19880916
 OS MARPAT 111:115749
 GI



AB Preparation of perindopril via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine. The title compound (I), useful as an antihypertensive (no data), is prepared, e.g., via N-acylation of perhydroindole derivative II (preparation given) with (S,S)-HO2CCHMeNHCHPrCO2Et (III). II-p-MeC6H4SO3H (preparation given) was condensed with III in EtOAc containing Et3N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to give, after deprotection and treatment with Me3CNH2, I.Me3CNH2.

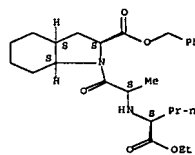
IT 122454-52-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and deprotection of)

RN 122454-52-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

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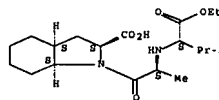
IT 107133-36-8P
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, via acylation of perhydroindole derivative with N-[(ethoxycarbonyl)butyl]alanine)
 RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMP C4 H11 N



IT 82834-16-0P, Perindopril

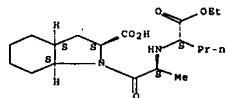
RL: SPN (Synthetic preparation); PREP (Preparation)

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(preparation of, via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine)
 RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LS ANSWER 178 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 1989:515738 CAPLUS Full-text
 DN 111:115738

TI Preparation of N-alkyl-α-amino acids and their derivatives as intermediates for carboxylalkyl dipeptides
 IN Vincent, Michel; Ballarda, Jean; Marchand, Bernard; Remond, Georges
 PA ADIR, Fr.
 SO Eur. Pat. Appl., 17 pp.
 CODEN: EPXXDW
 DT Patent
 LA French
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 309324	A1	19890329	EP 1988-402340	19880916
EP 309324	B1	19910313		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2620700	A1	19890324	FR 1987-12902	19870917
FR 2620700	B1	19900601		
CA 1341380	C	20020806	CA 1988-577079	19880907
DK 8805152	A	19890318	DK 1988-5152	19880915
DK 173730	B1	20010806		
AU 8822356	A	19890323	AU 1988-22356	19880916
AU 607260	B2	19910228		
JP 01110651	A	19890427	JP 1988-232122	19880916
JP 07025723	B	19950322		
ZA 8806932	A	19890530	ZA 1988-6933	19880916
AT 61567	T	19910315	AT 1988-402340	19880916
ES 2034324	T3	19930401	ES 1988-402340	19880916
JP 07206792	A	19950808	JP 1994-241178	19941005
JP 2524489	B2	19960814		
FR 1987-12902	A	19870917		
EP 1988-402340	A	19880916		
OS CASREACT 111:115738; MARPAT 111:115738				
GI				

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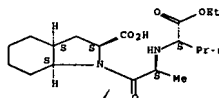


AB (S,S)-HO2CCHMeNHCHPrCO2R2 (I; R1,R2 = lower alkyl), useful as intermediates for carboxylalkyl dipeptides R3CO-Q-COCHMeNHCHPrCO2R2 (II; R3 = H, alkyl; Q = residue of indoline, isoindoline, tetrahydroquinoline, tetrahydroisoquinoline, etc.), especially perindopril and its deriva., are prepared via (S,S)-H2NCHMeO2CH2Ph (III) with XCHPrCO2R2 (IV; X = halo), separation of (S,S) isomer from the resulting V, and deprotection by hydrogenolysis. III (preparation given) was reacted with IV (X = Br) in DMF containing Et3N to give V (R1 = Pr, R2 = Et), from which the (S,S) isomer was separated. This was hydrogenolyzed to give (S,S)-I (R1 = Pr, R2 = Et).

IT 82834-15-0D, Perindopril, deriva.
 RL: RCT (Reactant); RACT (Reactant or reagent) (intermediates for, alkylamino acids as)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LS ANSWER 179 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
 AN 1989:477846 CAPLUS Full-text
 DN 111:77846

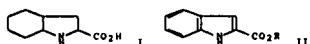
TI Industrial preparation of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid as intermediate for antihypertensive perindopril
 IN Vincent, Michel; Ballarda, Jean; Marchand, Bernard; Remond, Georges
 PA ADIR, Fr.
 SO Eur. Pat. Appl., 16 pp.
 CODEN: EPXXDW
 DT Patent
 LA French
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 308339	A1	19890322	EP 1988-402337	19880916
EP 308339	B1	19920506		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2620703	A1	19890324	FR 1987-12900	19870917
FR 2620703	B1	19911004		
DK 8805149	A	19890318	DK 1988-5149	19880915
AU 8822361	A	19890323	AU 1988-22361	19880916

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AU 618752 B2 19920109
 ZA 8806931 A 19890530 ZA 1988-6931 19880916
 US 4935525 A 19900419 US 1988-245352 19880916
 JP 02191251 A 19900727 JP 1988-232123 19880916
 AT 75731 T 19920515 AT 1988-402337 19880916
 ES 2033450 T3 19930316 ES 1988-402337 19880916
 US 4954640 A 19900904 US 1990-462797 19900110
 PRA1 FR 1987-12900 A 19870917
 EP 1988-402337 A 19880916
 US 1988-245352 A3 19880916
 OS CASREACT 111:77846; MARPAT 111:77846
 GI

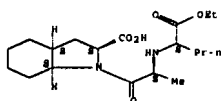


AB The title compound (I), useful as an intermediate for antihypertensive perindopril, was prepared from indolecarboxylic acid deriva. II (R = H, lower alkyl). Esterification of II (R = H) in EtOH containing H2SO4, reduction with Sn in EtOH containing HCl, saponification, and resolution gave (S)-indoline-2-carboxylic acid (III). Hydrogenation of III over Rh under H2 at 60° gave (2S,3aS,7aS)-octahydroindole-2-carboxylic acid.

IT 82834-16-0 167133 36-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (intermediate for, octahydroindolecarboxylic acid as)

RN 82834-16-0 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMP C19 H32 N2 O5

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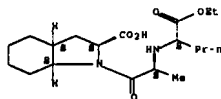
currently done using a radioimmuno. assay, but a mass fragmento-graphic method was developed using plasma spiked with the drugs, which were then derivatized to the iso-Bu ester heptofluorobutyramide and assayed using ammonia neg. chemical ionization. Levels of 100 pg/mL were assayed. However, isobutanol derivatization provoked partial transesterification of the Et ester of the parent drug into the diisobutyl ester derivative, which corresponds to the active metabolite. A second method of derivatization to stable trimethylsilyl esters preserved the original Et ester of the parent drug. Despite the lower ionization yields, the mass fragmentog. method was sensitive and accurate enough to work satisfactorily at the 2 ng/mL level in spiked plasma, which is the level found currently in patients.

IT 107133-36-8 167133 36-5
 RL: ANT (Analyte); ANST (Analytical study)
 (determination of, in blood plasma of humans by gas chromatog.-mass spectrometry, derivatization and ionization modes for)
 RN 107133-36-8 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
 CMP C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
 CMP C4 H11 N

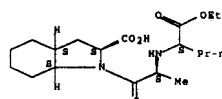


IT 120465-01-EP 120465-02-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 120465-01-2 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-[(ethoxycarbonyl)butyl] (2,2,3,3,4,4,4-heptafluoro-1-oxobutyl)amino]-1-oxopropyl]octahydro-, 2-methylpropyl

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Absolute stereochemistry. Rotation (-).

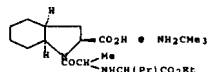


CM 2

CRN 75-64-9
 CMP C4 H11 N



L8 ANSWER 180 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM
 AN 1059:204950 CAPLUS Full-text
 DN 110:204950
 TI Gas chromatography-mass spectrometry of perindopril and its active free metabolite, an angiotensin convertase inhibitor: choice of derivatives and ionization modes
 AU Tsacanas, Christos; Devissaguet, Michele; Padieu, Prudent
 CS Cent. Spectrom. Masse, Fac. Med., Dijon, F-21033, Fr.
 SO Journal of Chromatography (1989), 488(1), 249-65
 CODEN: JOCRAM; ISSN: 0021-9673
 DT Journal
 LA English
 GI



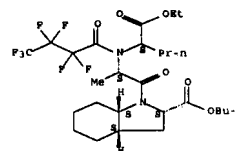
AB Perindopril (I), a perhydroindole compound and a novel class of angiotensin convertase inhibitor, after oral administration leads to an active metabolite by de-esterification of the Et ester. Routine biol. measurements are

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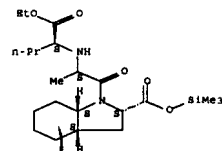
ester, [2S-[1(R*)],2α,3αβ,7αβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



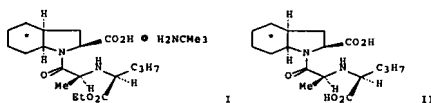
RN 120465-02-3 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, trimethylsilyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 181 OF 186 CAPLUS COPYRIGHT 2007 ACS on STM
 AN 1058:631529 CAPLUS Full-text
 DN 109:231529
 TI Synthesis of 89490-3 [U-14C-cyclohexyl] 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-(2S,3aS,7aS)-perhydroindole-2-carboxylic acid tert-butylamine salt and 89780 [U-14C-cyclohexyl] 1-[(2S)-2-[(1S)-1-(carboxybutyl)amino]-1-oxopropyl]-(2S,3aS,7aS)-perhydroindole-2-carboxylic acid and of [3,4-3H-butylamino]89490-3 and [(3,4-3H-butylamino]89780
 AU Pichat, L.; Tostain, J.; Gomis, J. M.; Coppo, M.; Moustier, A. M.; Vincent, M.; Remond, G.; Portevin, B.; Laubie, M.
 CS CEN Saclay, Gif sur Yvette, 91191, Fr.
 SO Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(5), 553-68
 CODEN: JLCRD4; ISSN: 0362-4803
 DT Journal
 LA French
 OS CASREACT 109:231529

GI



AB The title 14C-labeled compds. I (* signifies the uniform labeling of the cyclohexane ring with 14C) and II were prepared from aniline-U-14C in several steps. The title 3H-labeled compds. were also prepared. The latter synthesis involved the tritiation of an allylglycine residue. The title compds. are potent inhibitors of angiotensin-converting enzyme.

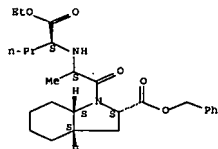
IT 117770-57-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrogenolysis of)

RN 117770-57-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)butyl)amino]-1-oxopropyl]octahydro-, phenylmethyl ester, labeled with carbon-14, [2S-[1(R*(R*),2a,3a,7a)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 117770-49-7P 117770-64-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and saponification of)

RN 117770-49-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)butyl)amino]-1-oxopropyl]octahydro-, labeled with carbon-14, [2S-[1(R*(R*),2a,3a,7a)]]-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 117770-48-6

CS Austin Hosp., Univ. Melbourne, Heidelberg, Australia
SO Arzneimittel-Forschung (1988), 38(5), 647-50
CODEN: ARZNAD; ISSN: 0004-4172

DT Journal

LA English

GI For diagram(s), see printed CA issue.

AB The biotransformation of di-acid angiotensin converting enzyme inhibitors perindopril (I), ramipril (II) and enalapril (III) to cyclized lactam metabolites was studied in the urine of rats using gas chromatog.-mass spectrometry. Chemical synthesis of the corresponding piperazinedione metabolites was achieved by reaction of I, II and III with Ac2O followed by hydrolysis of the ester group by Na in EtOH or by acid hydrolysis. Electron impact and chemical ionization mass spectra confirmed the structure of these potential novel metabolites. Selected ion monitoring of urinary excreta demonstrated small amts. (<5%) of these lactams for all 3 inhibitors. However, it was shown that the majority of these lactams were formed as a result of sample treatment rather than due to biotransformation.

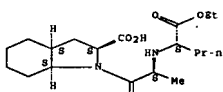
IT 82834-16-0, Perindopril

RL: PROC (Process) (biotransformation of, as diacid angiotensin converting enzyme inhibitor)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3a,7a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LB ANSWER 183 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1988:484848 CAPLUS Full-text

DN 109:484848

TI Neutral metalloendopeptidase inhibitors in the treatment of hypertension, compositions and kits containing the inhibitors, manufacture of the compositions, compounds of the compositions and their preparation

IN Haselanger, Martin F.; Sybertz, Edmund, Jr.; Neustadt, Bernard R.; Smith, Elizabeth M.

PA Schering Corp., USA

SO Eur. Pat. Appl., 167 pp.

CODEN: EPXXDM

DT Patent

LA English

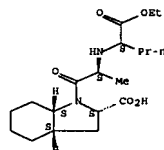
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 254032	A2	19880127	EP 1987-108730	19870617
EP 254032	A3	19900905		

R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE

OMP C19 H32 N2 O5
CIL XC-14

Absolute stereochemistry.



CM 2

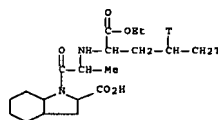
CRN 75-64-9

CMP C4 H11 N



RN 117770-64-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)butyl)-3,4-t2]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



LB ANSWER 182 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1988:485650 CAPLUS Full-text

DN 109:85650

TI Biotransformation studies of di-acid angiotensin converting enzyme inhibitors

AU Drummer, O. H.; Kourlis, S.; Iakovidis, D.

US 4749688	A	19880607	US 1986-876610	19860620
US 4801609	A	19890131	US 1987-32153	19870327
EP 566157	A1	19931020	EP 1993-107499	19870617
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FI 8702720	A	19871221	FI 1987-2720	19870618
AU 8774458	A	19871224	AU 1987-74458	19870618
AU 602701	B2	19901025		
ZA 8704413	A	19880224	ZA 1987-4413	19870618
HU 44940	A2	19880530	HU 1987-2786	19870618
IL 82908	A	19910916	IL 1987-62908	19870618
DK 8703138	A	19871221	DK 1987-3138	19870619
JP 2502589	A	19871221	NO 1987-2589	19870619
JP 63039855	A	19880220	JP 1987-153219	19870619
JP 2542620	B2	19961009		
JP 08283153	A	19961029	JP 1995-246555	19870619
US 5061710	A	19911029	US 1987-133669	19871216
AU 9068517	A	19910718	AU 1990-68517	19901227
AU 636423	B2	19930429		
US 4801609	B1	19931109	US 1991-90002282	19910214
US 5262436	A	19931116	US 1991-741025	19910806
JP 08176100	A	19960709	JP 1995-246554	19950821
PRAI US 1986-876610	A	19860620		
US 1987-32153	A	19870327		
EP 1987-108730	A	19870617		
JP 1987-153219	A3	19870619		
US 1987-133669	A3	19871216		

OS MRPAT 109:484848

AB Neutral metalloendopeptidase (NMEP) inhibitor is used alone or combined with an atrial peptide or an angiotensin converting enzyme (ACE) inhibitor for preparation of pharmaceutical compns. for treating hypertension. The compns. are obtained by mixing a NMEP inhibitor, alone or combined with an atrial peptide or ACE inhibitor, with a pharmaceutically acceptable carrier. 8-(4-Methylbenzyl)-L-cysteine, Me ester hydrochloride was prepared by adding thionyl chloride dropwise to N-tert-butyloxycarbonyl-S-(4-methylbenzyl)-L-cysteine in MeOH, heating the mixture under reflux for 90 min, cooling to room temperature, and concentrating in vacuo. Rats with induced hypertension were dosed a.c. with N-(N-[L-1-(2,2-dimethyl-1-oxopropoxy)methoxycarbonyl]-2-phenylethyl)-L-phenylalanine]-β-alanine and 1-[(2S)-3-mercapto-2-methyl-1-oxopropyl]-L-proline in Me cellulose vehicle to give a 1-, 2-, 3-, and 4-h decrease in blood pressure of 14, 19, 19, and 15 mmHg vs. an increase of 14, 11, 11, and 8 with the NMEP inhibitor alone and a decrease of 11, 7, 1, and 1 mmHg with the ACE inhibitor alone.

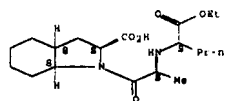
IT 82834-16-0, Perindopril

RL: BIOL (Biological study) (angiotensin converting enzyme inhibitor, antihypertensive containing neutral metalloendopeptidase inhibitor and)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3a,7a)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



10576386 357 of 361

AN 1987:470497 CAPLUS Full-text

DI 107:70497

TI Angiotensin-converting enzyme inhibitors: measurement of relative inhibitory potency and serum drug levels by radioinhibitor binding displacement assay

AU Jackson, Bruce; Cubela, Rose; Johnston, Colin I.

CS Austin Hosp., Univ. Melbourne, Heidelberg, 3084, Australia

SO Journal of Cardiovascular Pharmacology (1987), 9(6), 699-704

CODEN: JCPDCT; ISSN: 0160-2446

DT Journal

LA English

AB Radioinhibitor binding displacement, a new method for the measurement of angiotensin-converting enzyme (ACE) competitive inhibitors, has been used to assess the relative potency of 9 synthetic ACE inhibitors. MK351A, a tyrosyl derivative of enalaprilic acid was iodinated with ¹²⁵I and used as the radioligand. [¹²⁵I]-MK351A bound to human serum ACE in a concentration-dependent manner. It was displaced in a concentration-dependent manner by all ACE inhibitors tested. Fifty percent displacement of bound [¹²⁵I]-MK351A (ID₅₀) for each ACE inhibitor correlated well with inhibitor potency ID₅₀, estimated using an ACE enzymic activity assay using Hip-His-Leu as substrate. The radioinhibitor binding displacement assay was used to measure serum concentration of enalaprilic acid (MK422) in human serum samples. Drug concentration estimated by radioinhibitor binding displacement assay correlated closely with the drug concentration measured by a specific radioimmunoassay. The radioinhibitor binding displacement technique using [¹²⁵I]-MK351A as the ligand for human serum ACE has general application to all competitive ACE inhibitors, allowing comparison of in vitro ACE inhibitor potencies and estimation of serum ACE inhibitor concns.

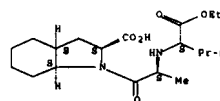
IT 2244-16-0, 89490

RL: B10L (Biological study)
(angiotensin-converting enzyme of blood serum of humans inhibition by, assay for determining)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



10576386 358 of 361

AN 1982:616716 CAPLUS Full-text

DI 97:216716

TI Substituted imino diacids and pharmaceutical preparations containing them

IN Remond, Georges; Laubie, Michel; Vincent, Michel

PA Science Union et Cie., Societe Francaise de Recherche Medicale, Fr.

SO Eur. Pat. Appl., 38 pp.

CODEN: EPXDXW

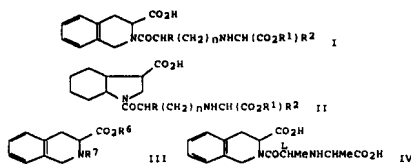
DT Patent

LA French

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 49658	A1	19820414	EP 1981-401501	19810929
EP 49658	B1	19840613		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
FR 2491469	A1	19820409	FR 1980-21095	19801002
FR 2491469	B1	19830513		
FR 2503155	A2	19821008	FR 1981-6916	19810407
FR 2503155	B2	19830701		
IL 63940	A	19850630	IL 1981-63940	19810925
AT 7910	T	19840615	AT 1981-401501	19810929
FI 8103034	A	19820403	FI 1981-3034	19810930
FI 77230	B	19881031		
FI 77230	C	19890210		
DK 8104343	A	19820403	DK 1981-4343	19811001
DK 157011	B	19891030		
DK 157011	C	19900326		
NO 8103339	A	19820405	NO 1981-3339	19811001
NO 160780	B	19890220		
NO 160780	C	19890531		
AU 8175949	A	19820408	AU 1981-75949	19811001
AU 542611	B2	19850228		
HU 28405	A2	19831228	HU 1981-2838	19811001
HU 185147	B	19841228		
SU 1553827	A3	19850430	SU 1981-3344196	19811001
CA 1341196	C	20010306	CA 1981-387093	19811001
JP 57091974	A	19820608	JP 1981-157367	19811002
JP 01032239	B	19890629		
ZA 106844	A	19820929	ZA 1981-6844	19811002
ES 505999	A1	19830416	ES 1981-505999	19811002
US 4508729	A	19850402	US 1981-308234	19811002
US 4565819	A	19860121	US 1982-420005	19820920
US 4616029	A	19861007	US 1984-659275	19841010
US 4616031	A	19861007	US 1984-659276	19841010
US 4644008	A	19870217	US 1984-659274	19841010
US 4616030	A	19861007	US 1984-679320	19841206

PRA1 FR 1980-21095 A 19801002
FR 1981-6916 A 19810407
FR 1979-30046 A 19791207
FR 1980-16875 A 19800731
US 1980-212607 A2 19801203
EP 1981-401501 A 19810929
US 1981-308234 A1 19811002
OB CABBREACT 97:216716; MARPAT 97:216716
GI



AB Heterocyclic amino acid deriva. I and II [R = C1-4 alkyl; R1 = H, C1-4 alkyl; R2 = alkyl, mono- or dicycloalkylalkyl, phenylalkyl, (CH2)mXCH2R3R4 (R3 = H, C1-4 alkyl, C3-6 cycloalkyl; R4 = H, C1-4 alkyl, C3-6 cycloalkyl, alkoxy-carbonyl; X = S, NR5 (R5 = H, Ac, CO2CH2Ph), m = 1, 2; n = 0, 1] were prepared. Thus, (S)-phenylalanine was cyclized with H2CO to give (S)-isoquinoline (S)-III (R6 = R7 = H), which was esterified with MeOH/HCl2 and then condensed with Boc-L-Ala-OH (Boc = MeCO2C) by DCC/1-hydroxybenzotriazole to give (S)-III (R6 = Me, R7 = Boc-L-Ala). The latter was saponified and then Boc-deblocked by CF3CO2H to give (S)-III (R6 = H, R7 = H-L-Ala), which was treated with MeCO2CH2 and then reduced by NaBH3CN to give isoquinoline (2S)-IV. I and II were useful as therapeutic agents due to their ability to inhibit enkephalinase, carboxypeptidase, kininase, and angiotensin-converting enzyme (ACE); e.g., the compds. can be used as antihypertensives since they inhibit ACE.

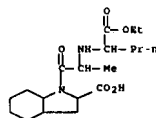
IT 82978-68-5P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

RN 82978-68-5 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)butyl]amino)-1-oxopropyl]octahydro-, (9CI) (CA INDEX NAME)



10576386 360 of 361

AN 1982:510360 CAPLUS Full-text

DI 97:110760

TI Stereoselective synthesis of a new perhydroindole derivative of chiral iminodiacid, a potent inhibitor of angiotensin converting enzyme

AU Vincent, M.; Remond, G.; Portevin, B.; Serkiz, B.; Laubie, M.

CS Inst. Rech. Servier, Suresnes, 92150, Fr.

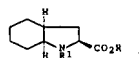
SO Tetrahedron Letters (1982), 23(16), 1677-80

CODEN: TETLEY; ISSN: 0040-4039

DT Journal

LA English

GI



AB The title enzyme inhibitor I (R = H, R1 = S,S-COCHMeNHCHPrCO2Et) (II) was prepared by coupling reaction of I (R = Me3, R1 = H) (III) with (S,S)-H2OCHMeNH-H2CHPrCO2Et Cl- (IV). III was stereoselectively prepared from (S)-2-carboxyindoline in 5 steps; IV was stereoselectively prepared by reaction of PrCO2CH2 with (S)-H2NCHMeCO2Me3 or by reaction of (S)-PrCH(CO2Et)N-H3 Cl- with MeCO2CH2. II showed 40% angiotensin converting enzyme inhibition after 24-30 h in dogs treated with 1 mg/kg p.o.

IT 82834-16-0P

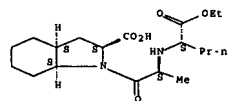
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and angiotensin converting enzyme inhibition by)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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COST IN U.S. DOLLARS

SINCE FILE TOTAL

ENTRY SESSION

FULL ESTIMATED COST

981.63 1175.64

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL

ENTRY SESSION

CA SUBSCRIBER PRICE

-145.08 -145.08

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 11:29:22 ON 28 NOV 2007